

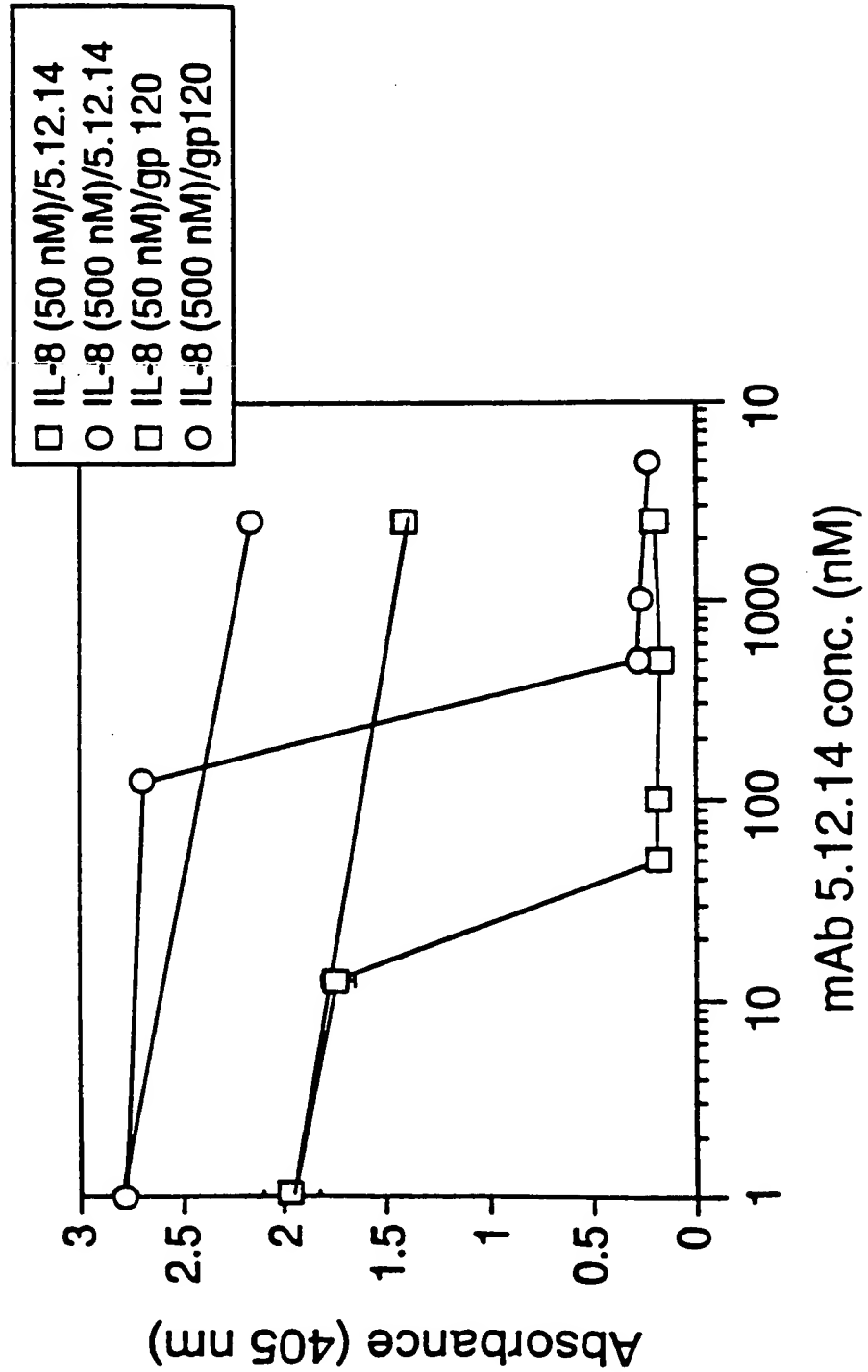


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 1



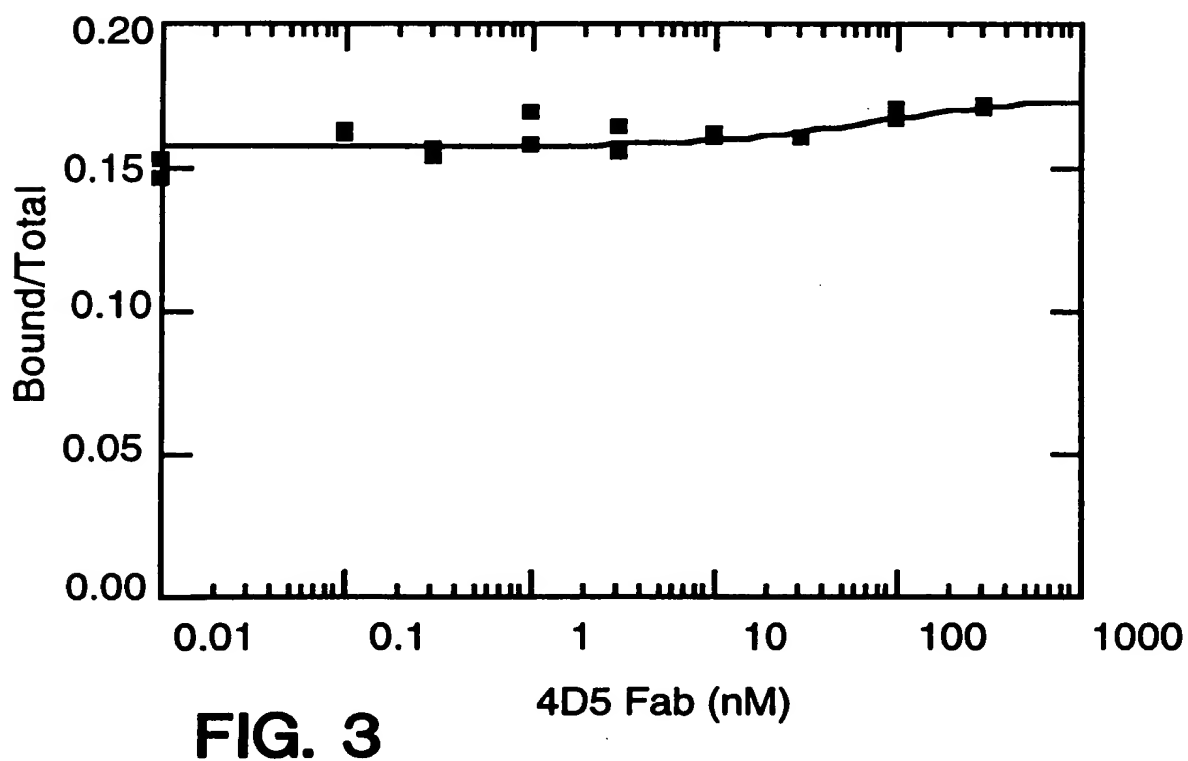
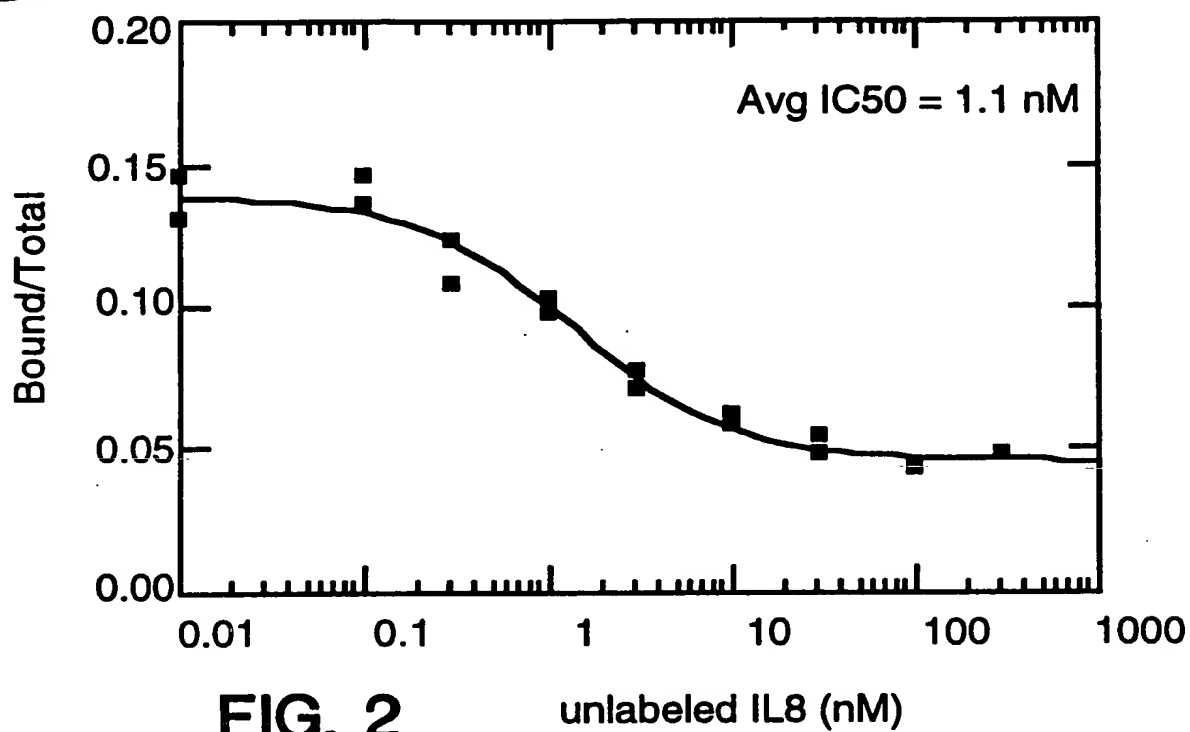


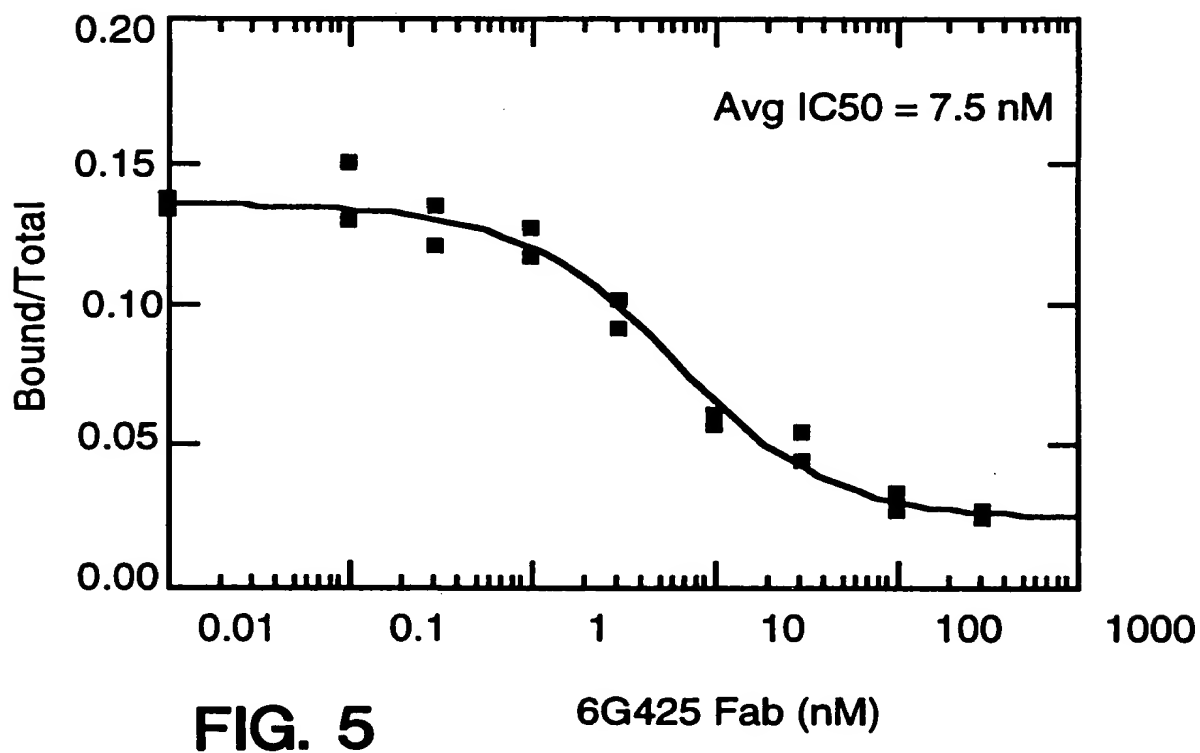
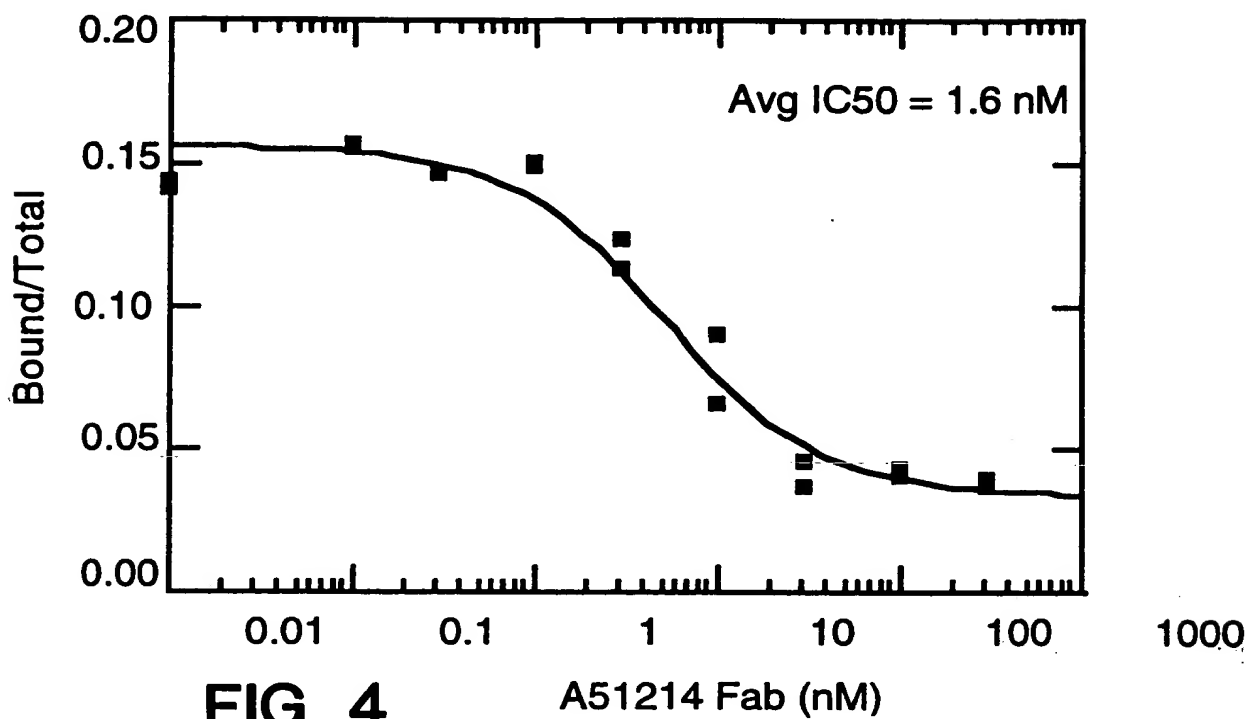
ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A







ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

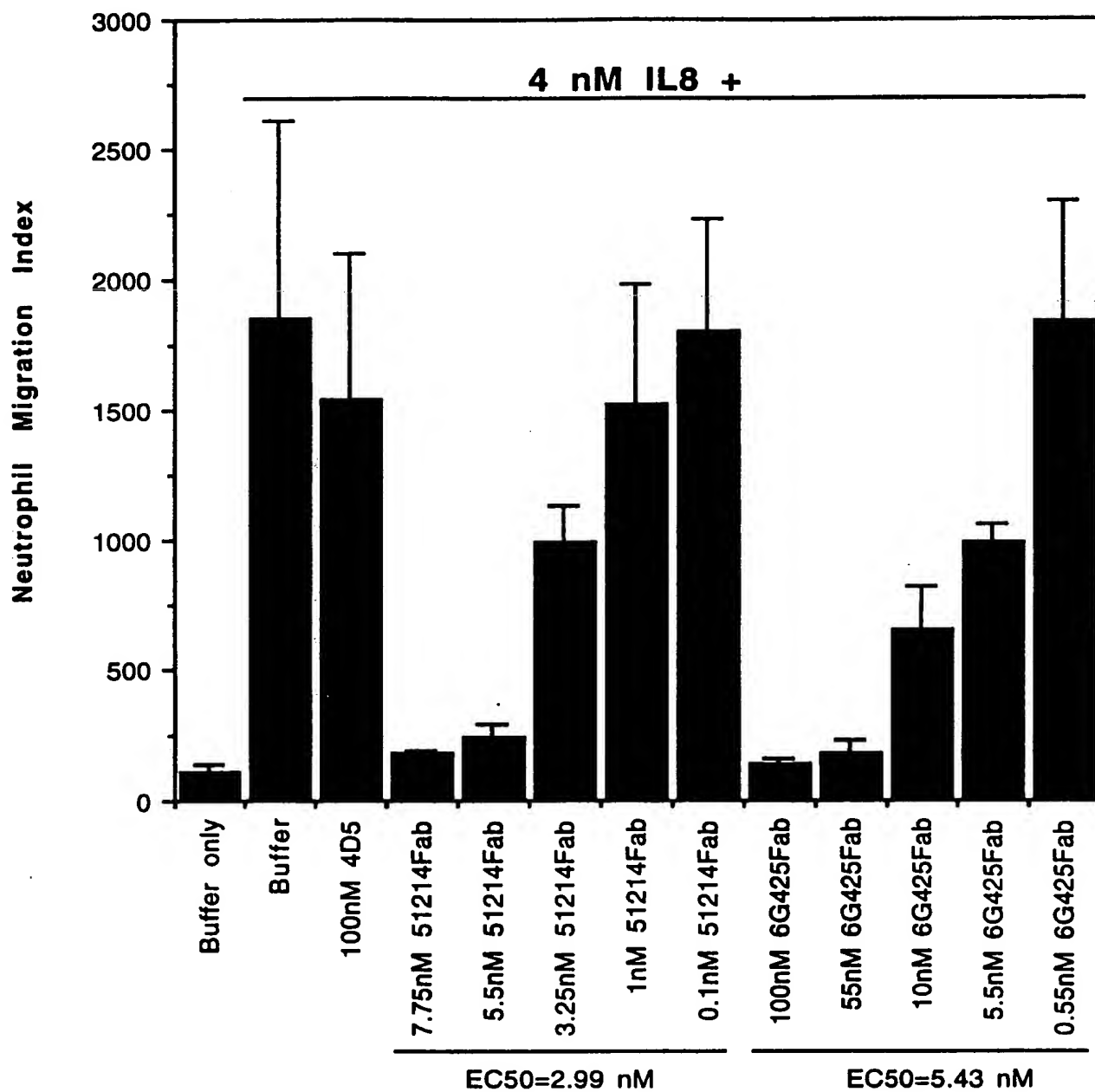


FIG. 6



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

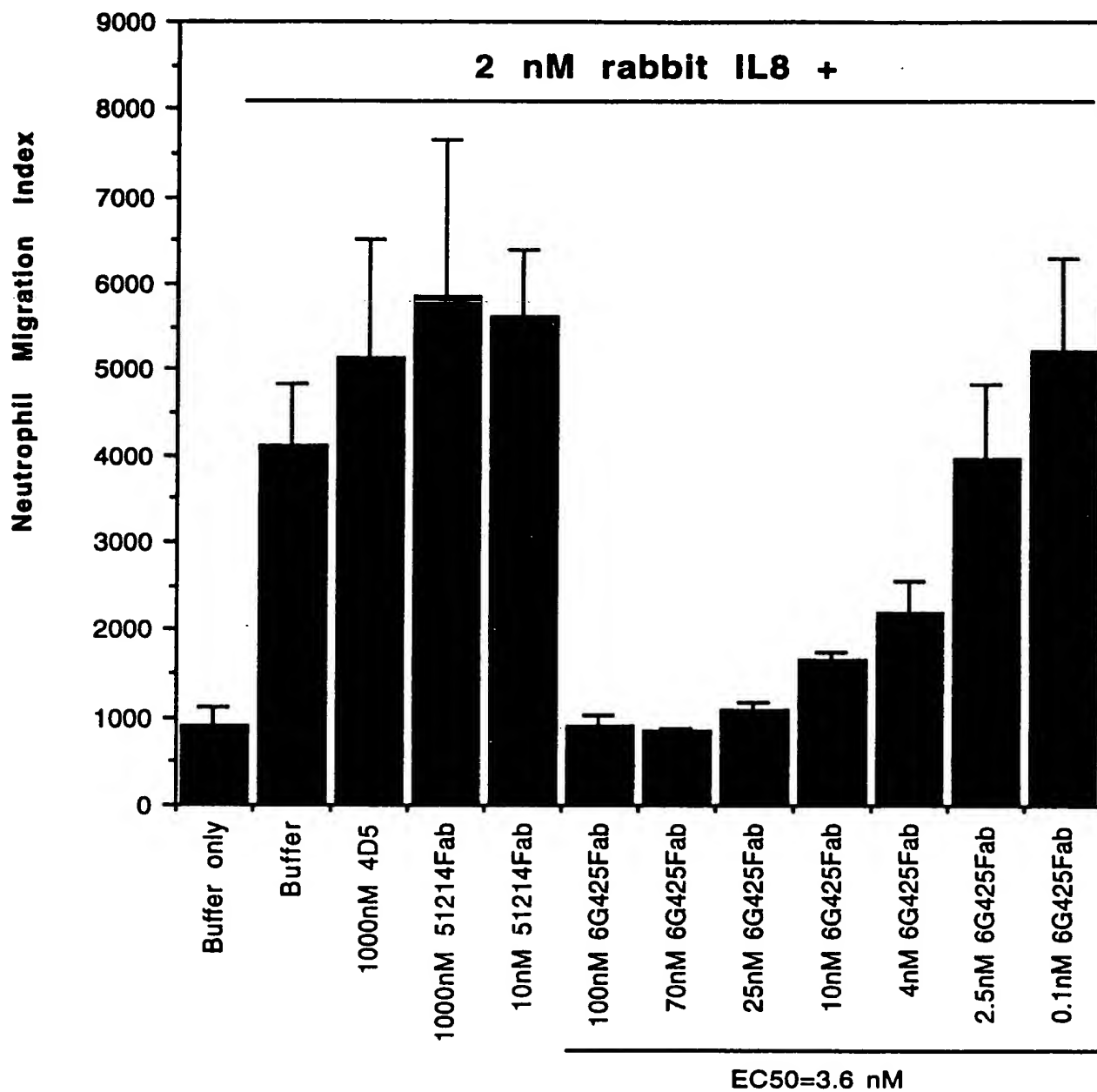


FIG. 7

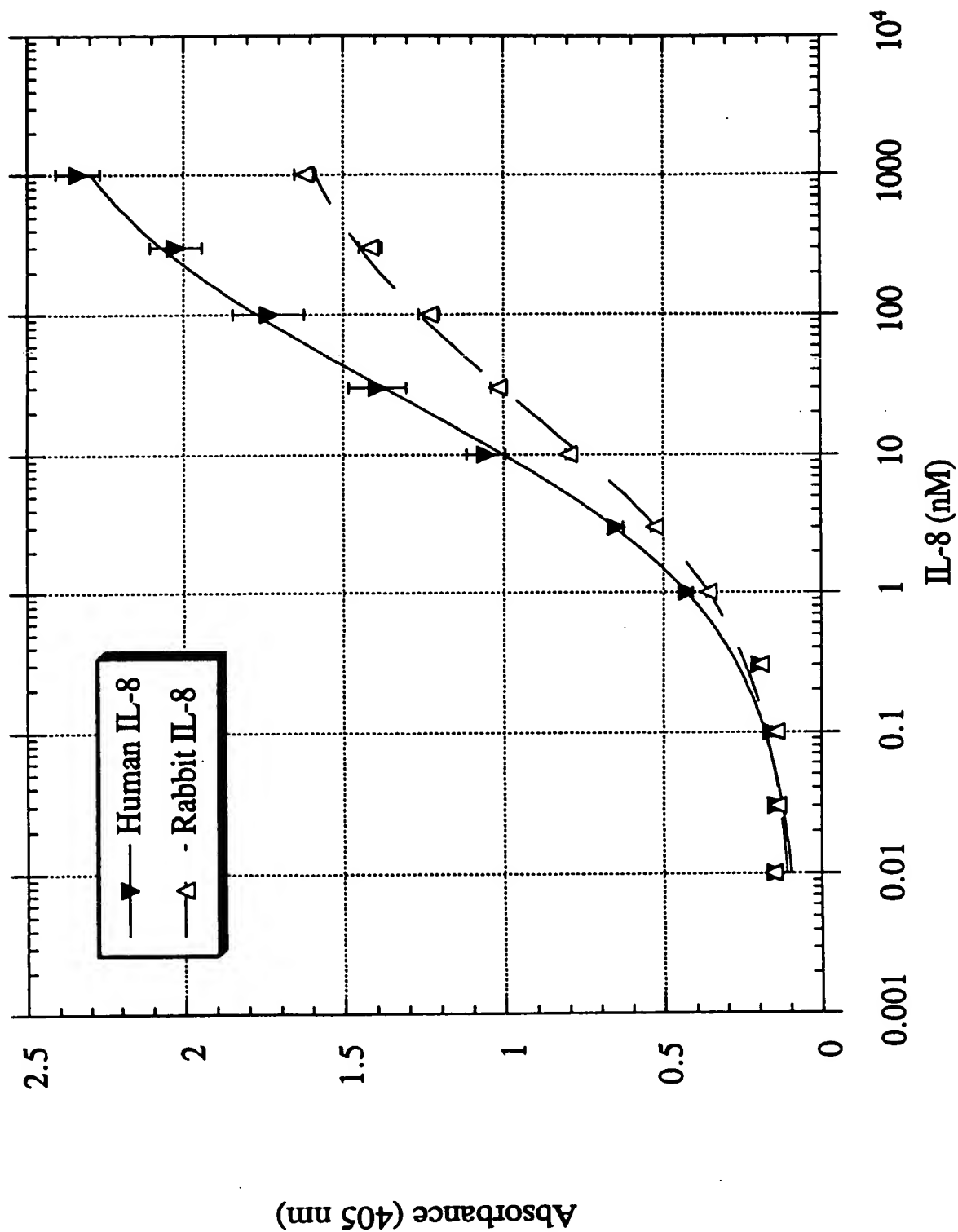


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 8



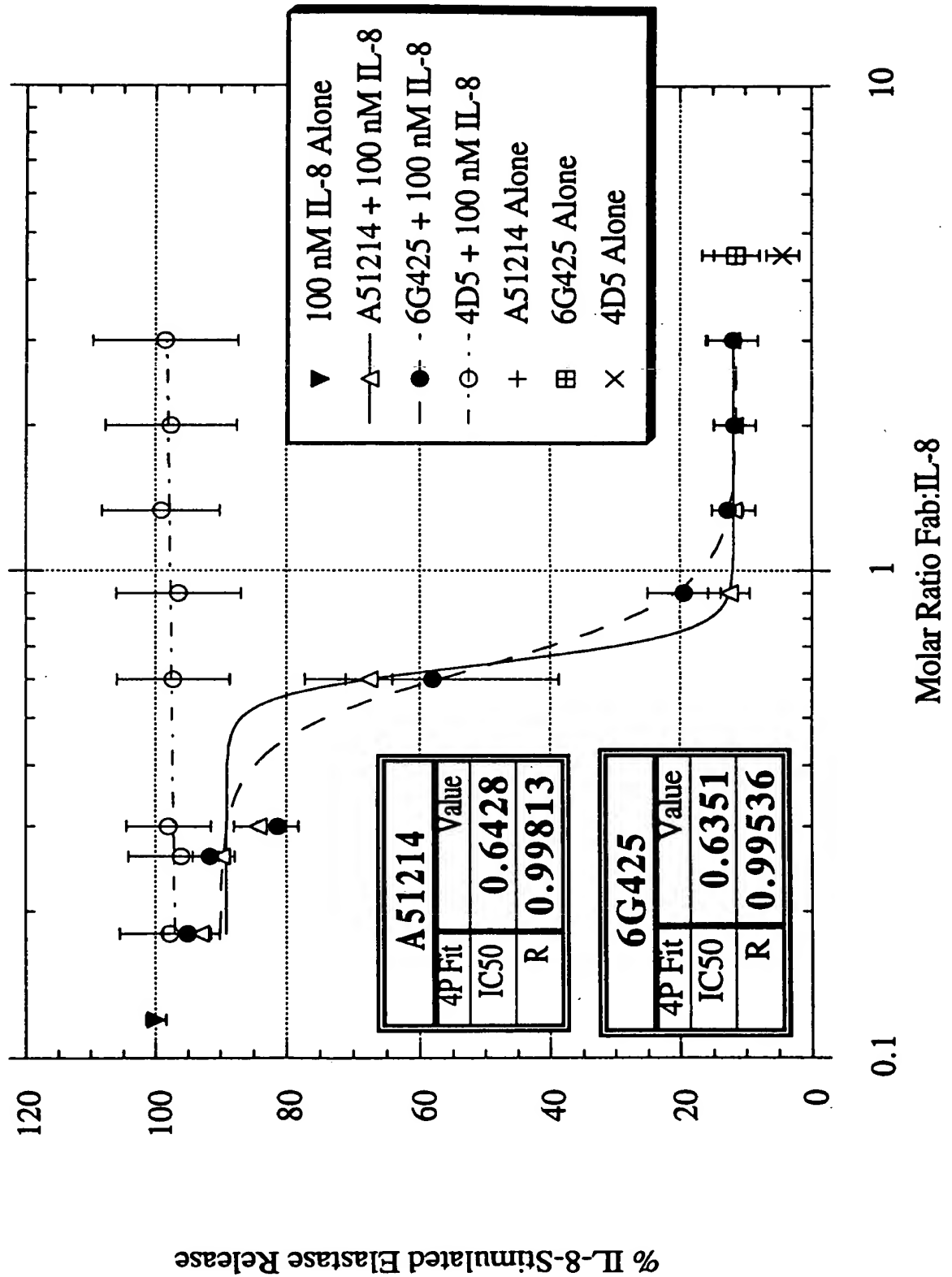


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 9



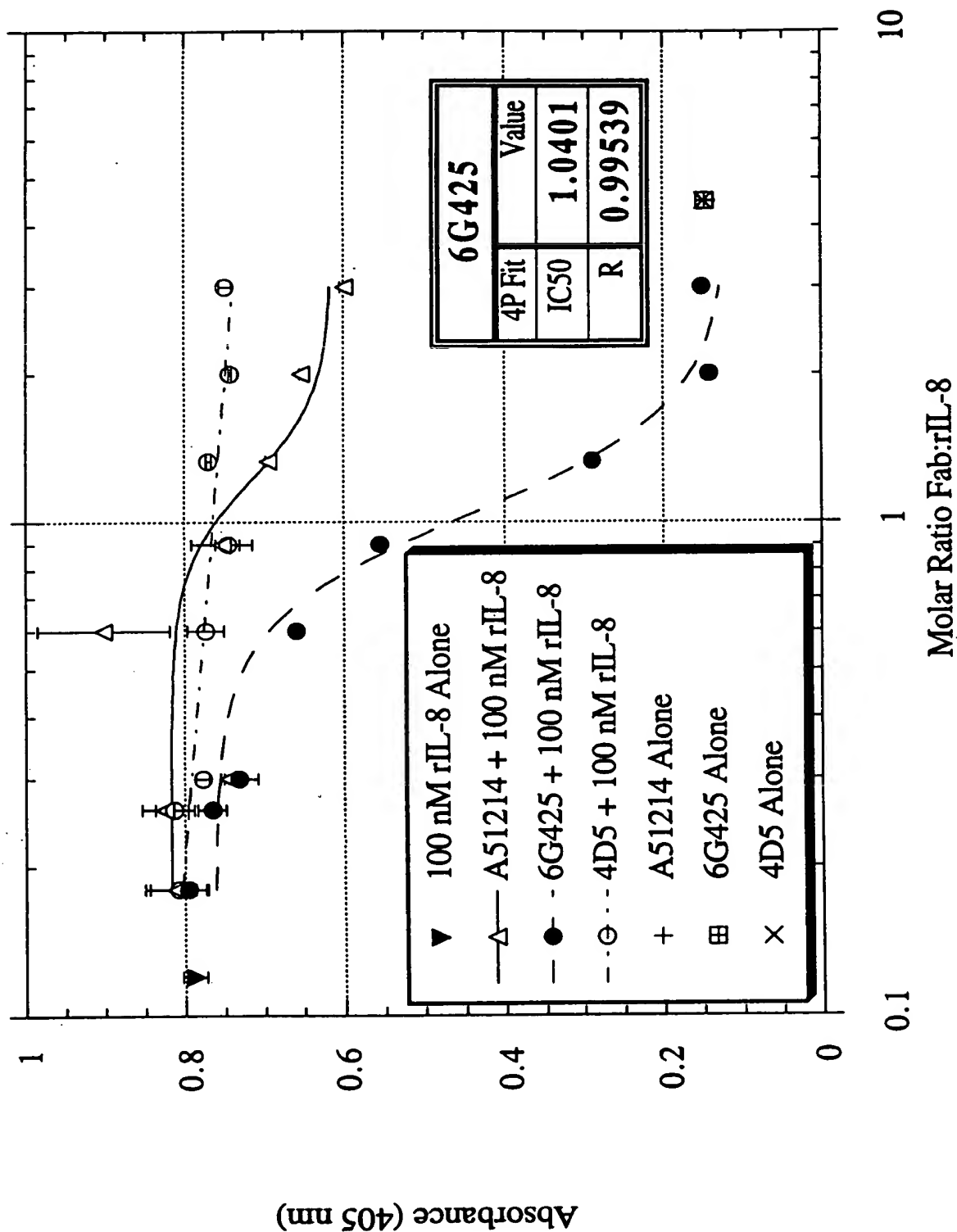


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 10





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

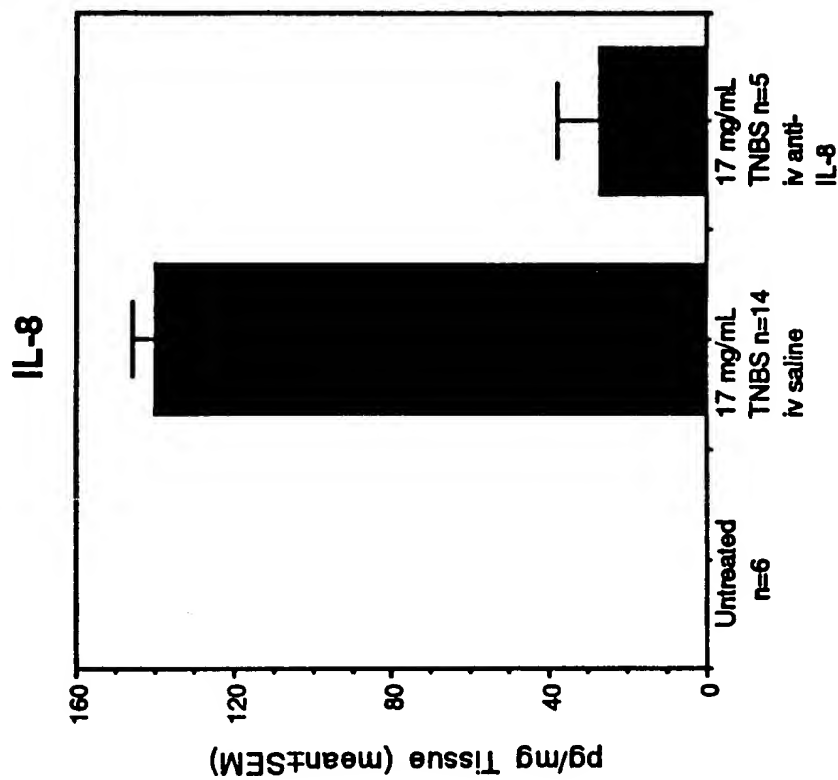


FIG. 11B

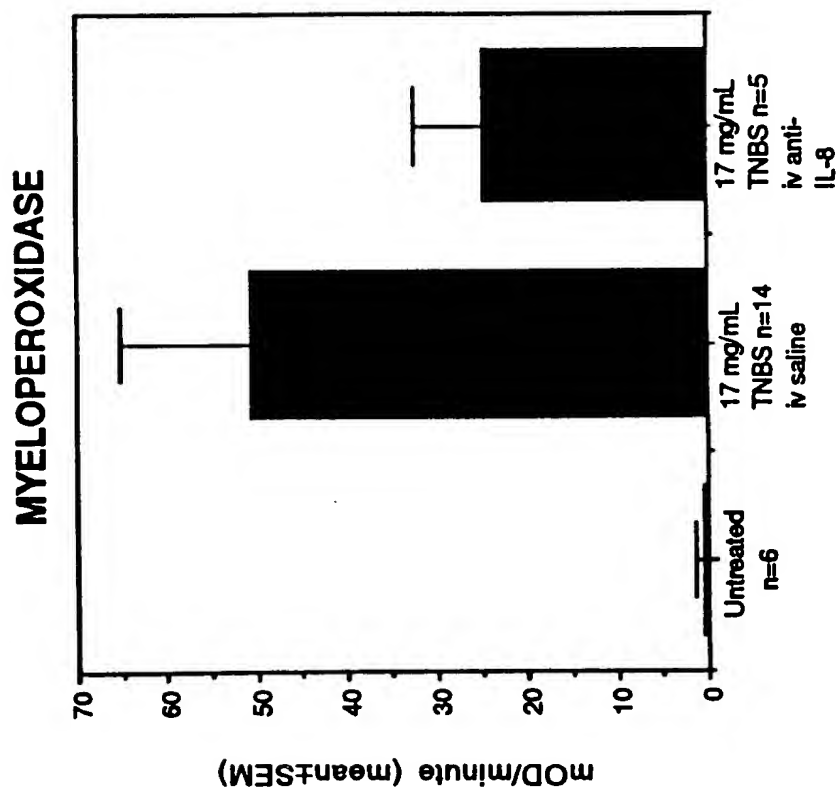


FIG. 11A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

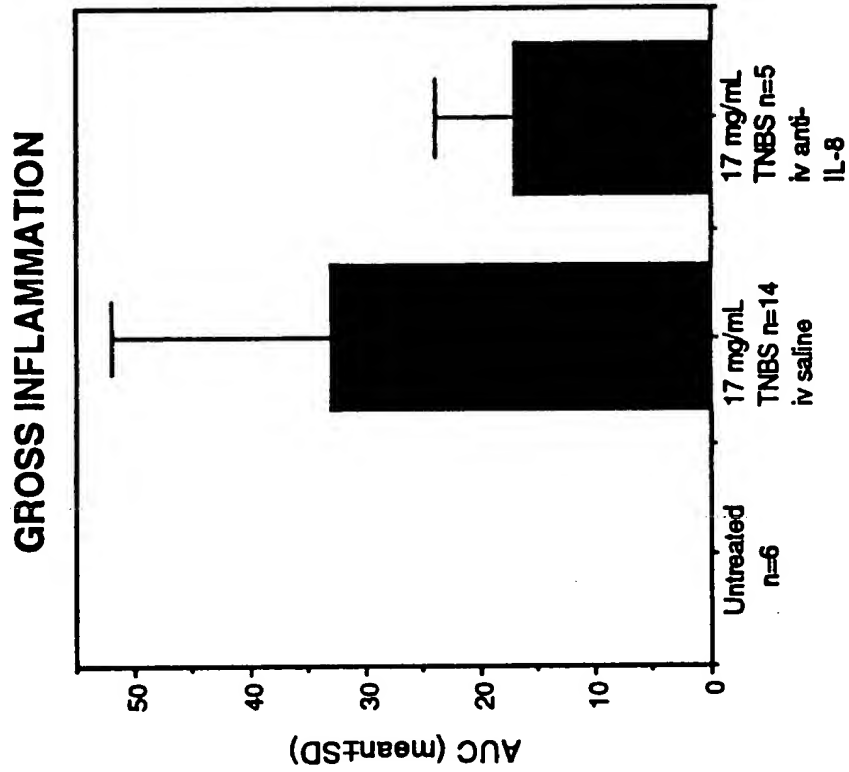


FIG. 11D

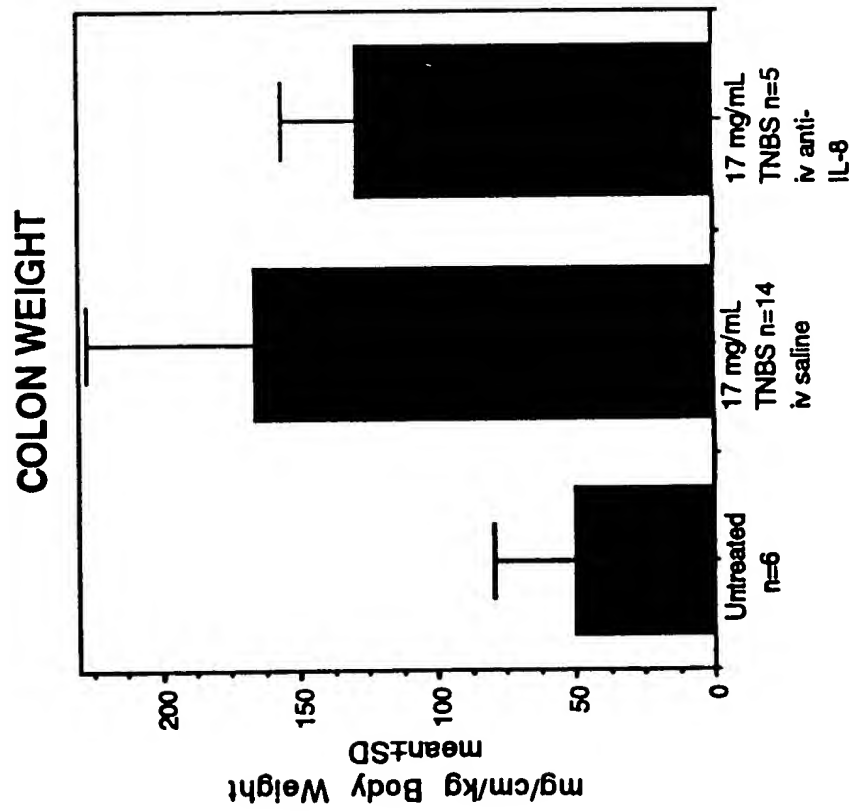


FIG. 11C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

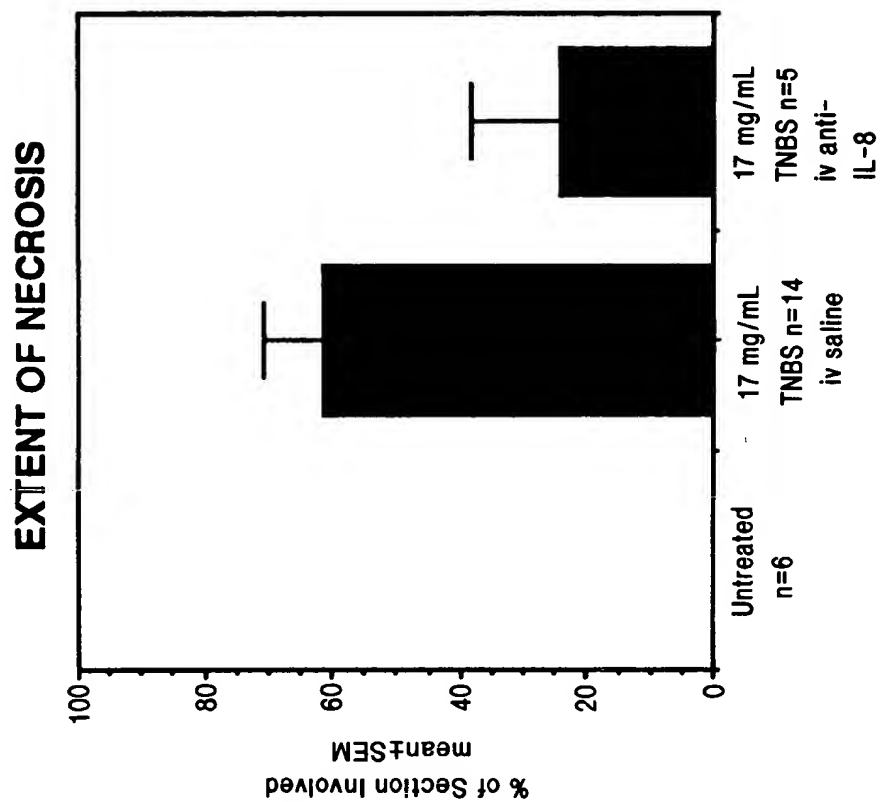


FIG. 11F

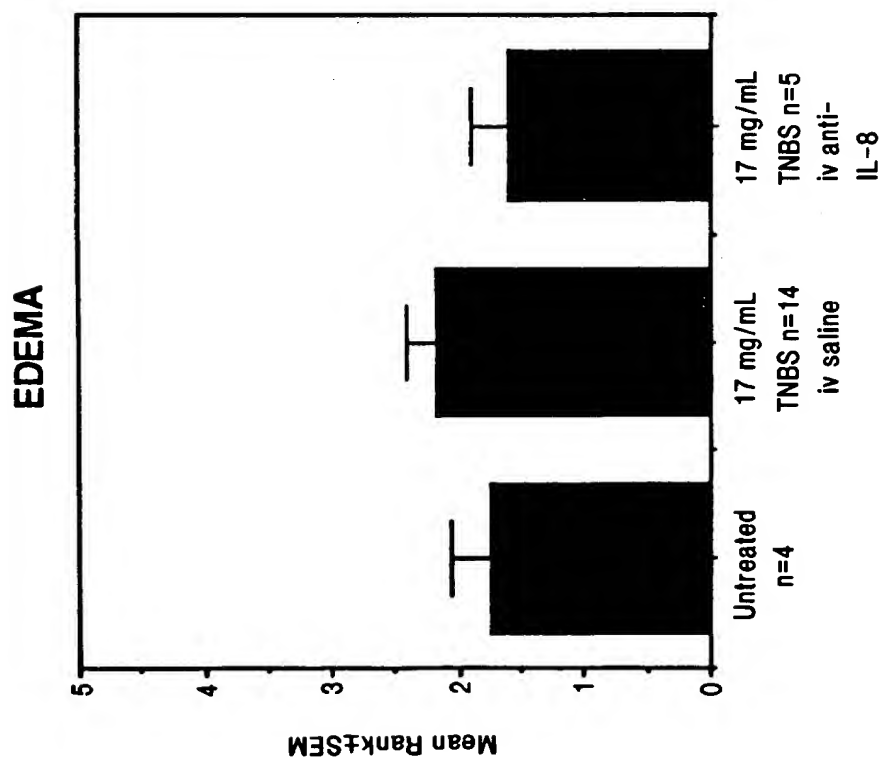
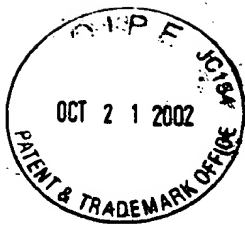


FIG. 11E



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

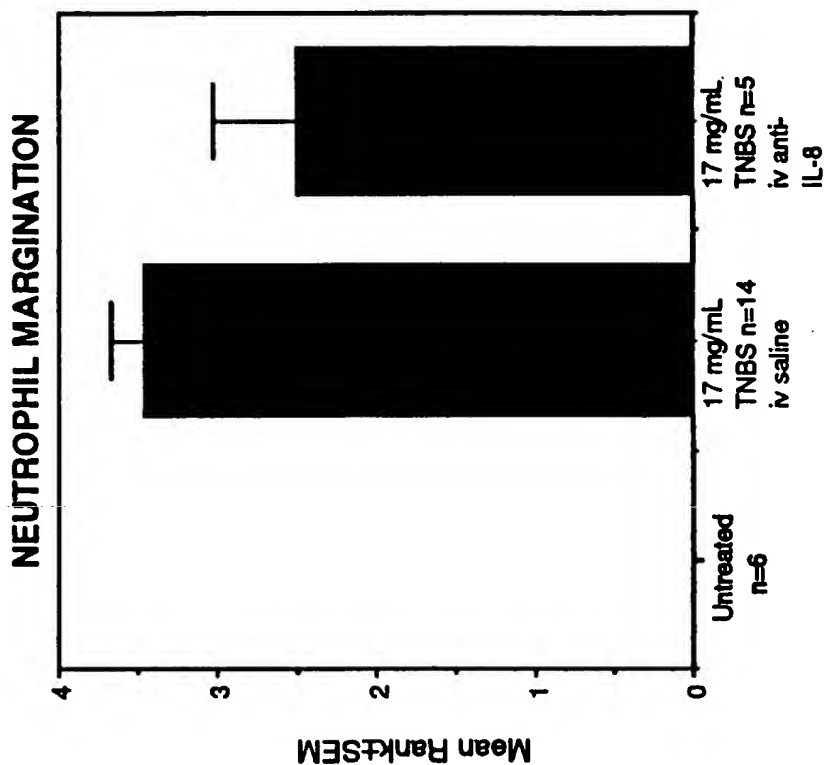


FIG. 11H

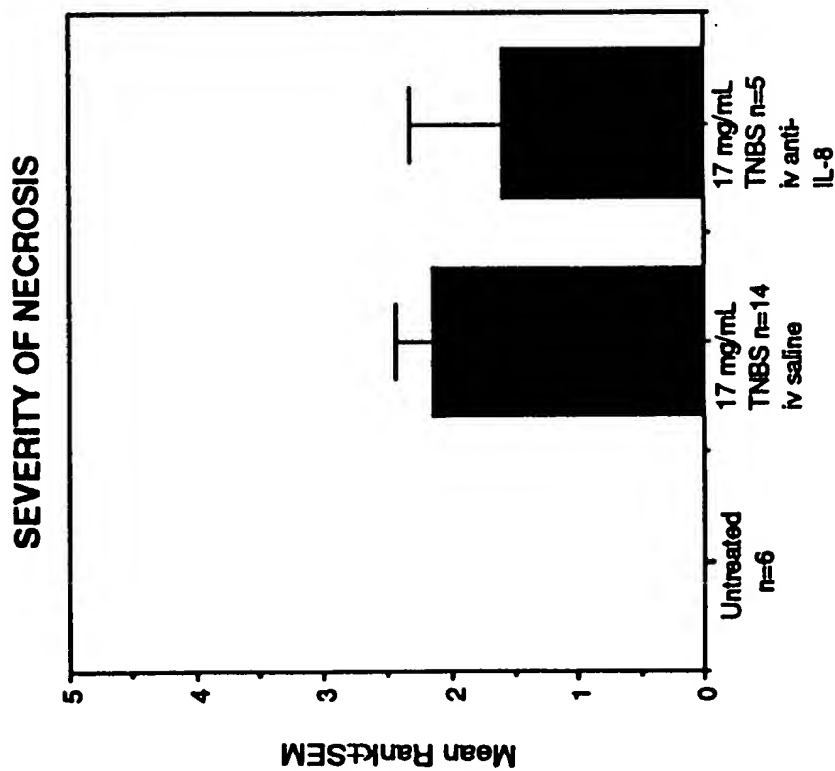


FIG. 11G



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

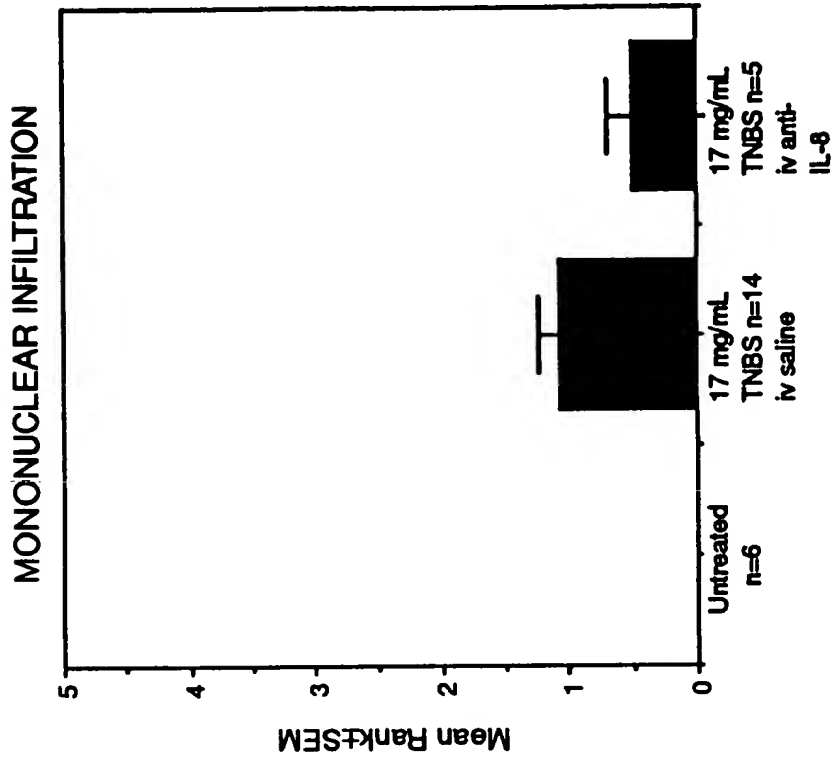


FIG. 11J

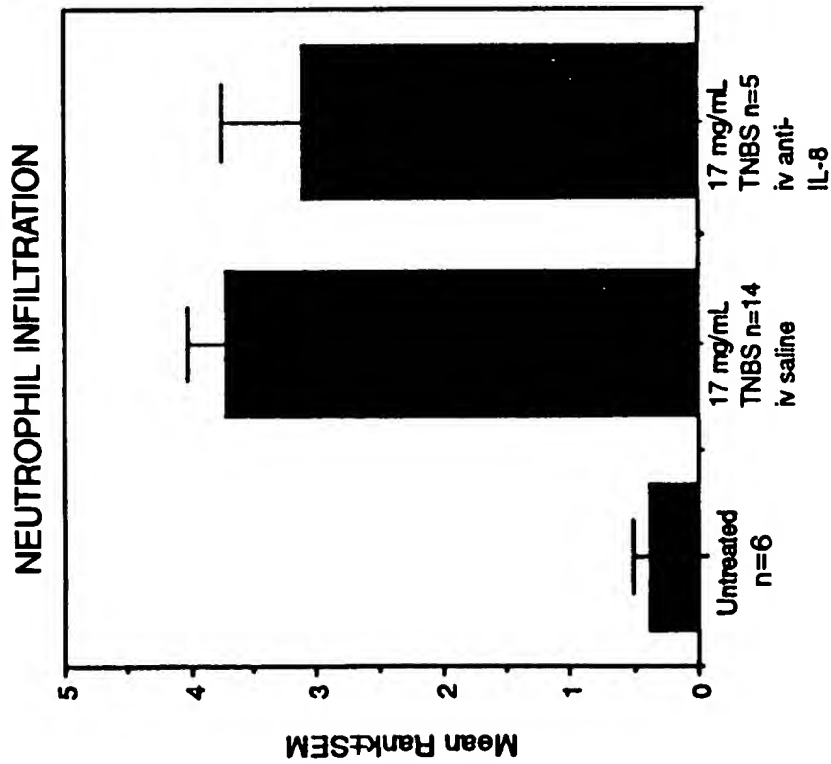


FIG. 11I

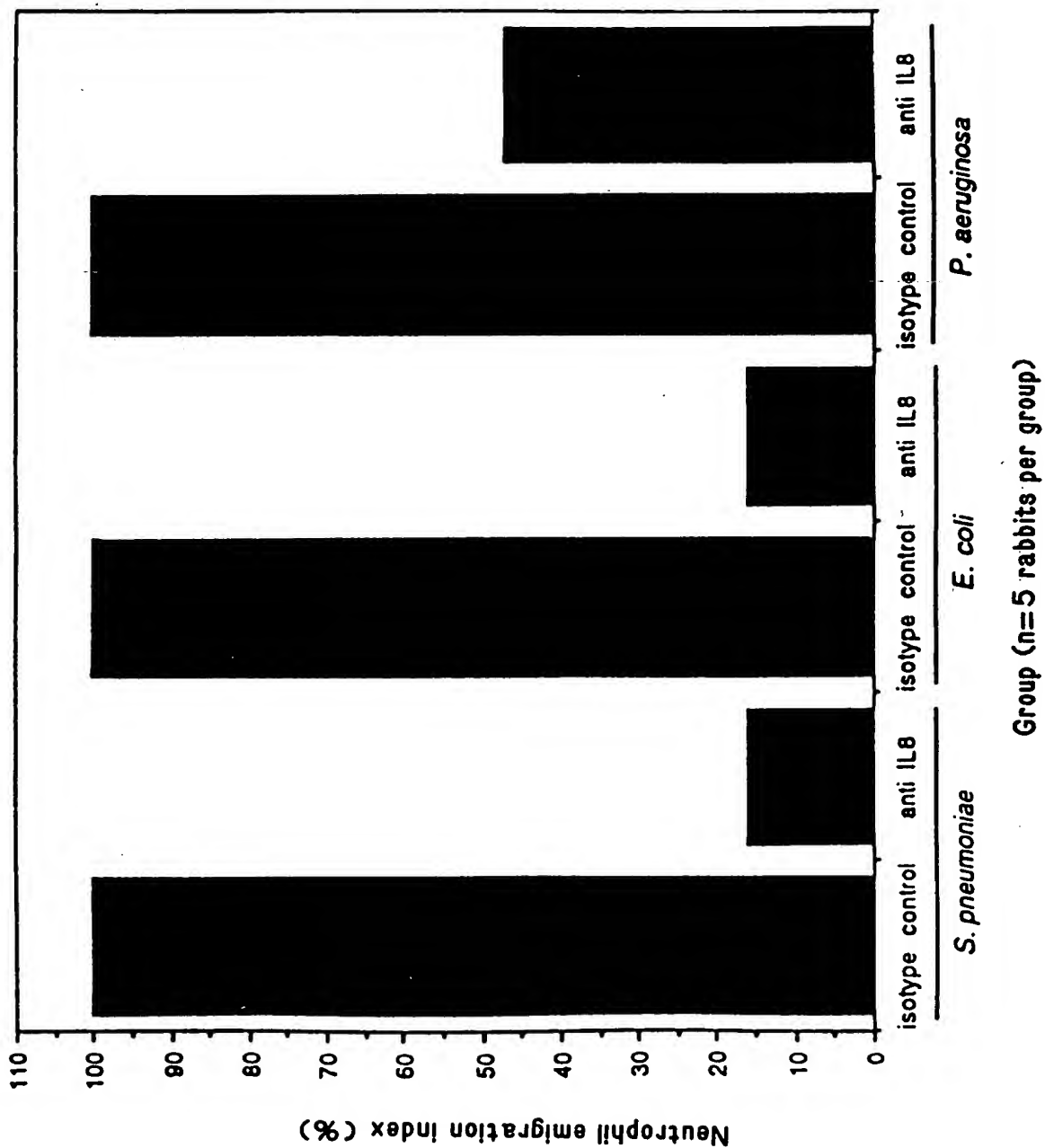


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 12





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Light Chain Primers:

MKLC-1, 22mer

FIG. 13

5' CAGTCCAAGTGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGCC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 14

Light chain forward primer

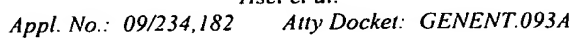
SL001A-2 35 mer

5' ACAACGCGTACGCT GACATCGTCATGACCCAGTC 3' (SEQ ID NO.7)
T T T
A (SEQ ID NO.8)
(SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3' (SEQ ID NO.10)



5' CGATGGCCCCG ATAGACCGATGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES
Hsei et al.
Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 GACATTGTCA TGACACAGTC TCAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTAAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCCTTTGGT
21 V T C K A S Q N V G T N V A W Y Q Q K P

CDR #1

121 GGGCAATCTC CTAAAGCACT GATTTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCGTTAGAG GATTTCTGTA CTAAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
CGGAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTCCCA
CCCTGGTTCG ACCTCAACTT TGCCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA (SEQ ID NO.16)

GGTAAGCTT

121 P F E (SEQ ID NO.17)

FIG. 16



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTGCGCA TGC GACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCTG CAACCATTA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACGG TTCTTGTTGGG ACATGGACGT TTA CTGTCGTA GACTTCAGAC TCCTGTGTCTG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCACTGTCT CTGCAGCCAA AACAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCTGG GGTAGACAGA
113 G T L V T V S A A K T T A P S V Y

411 ^{ApaI} ATCCGGG (SEQ ID NO.18)
TAGGCCC
130 P (SEQ ID NO.19)

FIG. 17



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTCTGTAC TAAATGAGCA GTAGGATGGC CATGTCACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTCAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTGGTT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCTCG TCGTTCCTGT CGTGGATGTC GGAGTCGTGC
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

711 TTAA (SEQ ID NO.24)
AATT
216 O

FIG. 19



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTTTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCGG ACCTCCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTCACTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTTTETC GGAGCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAAGTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

661 ACCGAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K
721 GTTGAGCCCA AATCTTGTA CAAACTCAC ACATGA (SEQ ID NO.26)
CAACTCGGT TTAGAACACT GTTTGAGTG TGTACT
218 V E P K S C D K T H T O (SEQ ID NO.27)

FIG. 20B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACTGTTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Light chain forward primer

6G4.light.Nsi 36-MER

5'	CCAATGCATACGCT	GAC	ATC	GTG	ATG	ACC	CAG	ACC	CC	3'	(SEQ ID NO.28)
		T	T			T			T		(SEQ ID NO.29)
						A			A		(SEQ ID NO.30)

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

FIG. 22



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T A G (SEQ ID NO.15)
(SEQ ID NO.14)
(SEQ ID NO.13)

FIG. 23



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *
CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *
CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *
CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT
98 H V P L T F G A G T K L E L K R A D A A
* * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34)
GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT

118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70 G AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTCG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII ApaI
421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCTG GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC (SEQ ID NO.36)

GTAG

135 I (SEQ ID NO.37)

FIG. 25



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *

38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #3

601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCTGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCGGACTCG AGCGGCAGT GTTCTCGAA GTTGTCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAA (SEQ ID NO.41)

CTCACAATT

218 E C O (SEQ ID NO.42)

FIG. 27B

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTCTG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

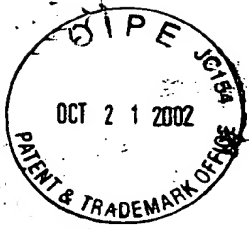
421 GTCACCGTCT CCTCCGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
TTCTCGTGGA GACCCCCGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCCGGCT
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTTCG CGCACGTGTG GAAGGGCCGA
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTGC
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

661 TTGGGCACC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCGTGG TCTGGATGTA GACGTTGCAC TTAGTGTTTCG GGTCGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA (SEQ ID NO.43)
TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTA CT
218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Variable Light Chain Domain

```

      10      20      abcde 30      40
6G425  DIVMTQTPLSLPVSLGDAQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
F(ab)-1  DIQMTQSPSSLSASVGDRTVITCRSSQSLVHGIGNTYLHWYQKPGKAPKLLIY
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
humkI    DIQMTQSPSSLSASVGDRTVITCRASKTI-----SKYLAWYQKPGKAPKLLIY
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
      =====
      ++++++++
      L1

      50      60      70      80      90      100
6G425  YKVSNRFGVDPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR (SEQ ID NO.45)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
F(ab)-1  YKVSNRFGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (SEQ ID NO.46)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
humkI    YSGSTLESVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR (SEQ ID NO.47)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
      =====
      ++++++++
      L2                               ++++++++
      L3
```

Variable Heavy Chain Domain

```

      10      20      30      40
6G425  EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVWKQSHGKSLEWI
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
F(ab)-1  EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVWRQAPGKGLEWV
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
humIII   EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWRQAPGKGLEWV
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
      =====
      ++++++
      H1

      50  a      70      80  abc      90      100      110
6G425  GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT (SEQ ID NO.48)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
F(ab)-1  GYIDPSNGETTYNQKFKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT (SEQ ID NO.49)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
humIII   GMIHPSDSETRYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGIIFY-GTTYFDYWGQGT (SEQ ID NO.50)
      #   #   #   #   #   #   #   #   #   #   #   #   #   #   #
      =====
      ++++++++
      H2                               ++++++++
      H3
```

FIG. 29



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

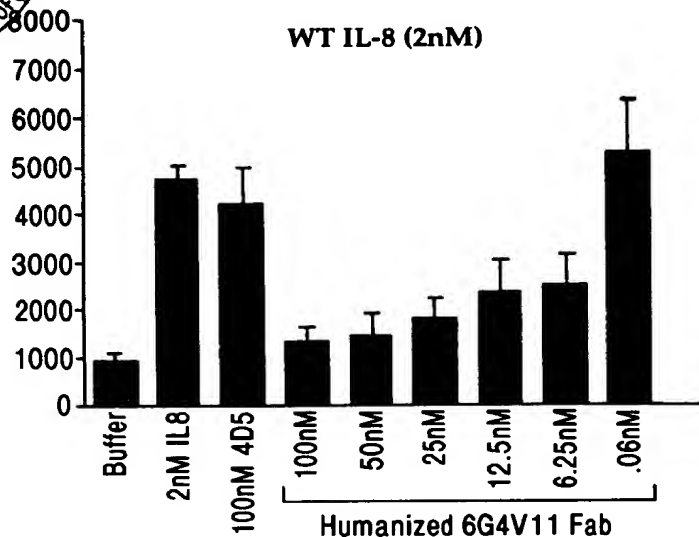


FIG. 30A

IC₅₀~12nM

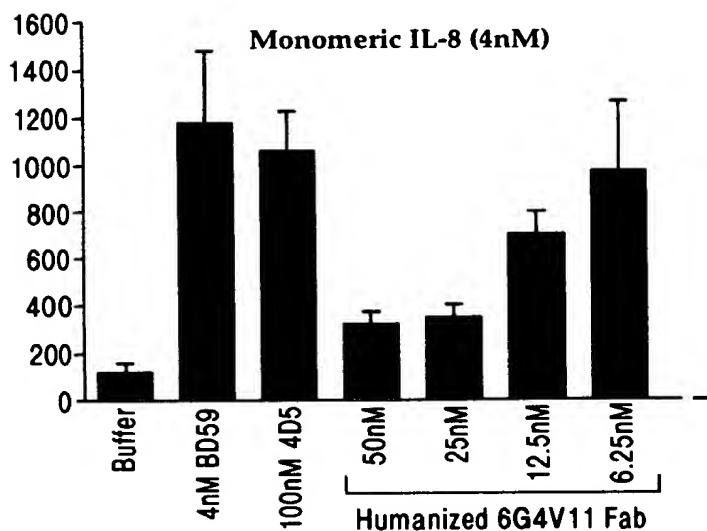


FIG. 30B

IC₅₀~15nM

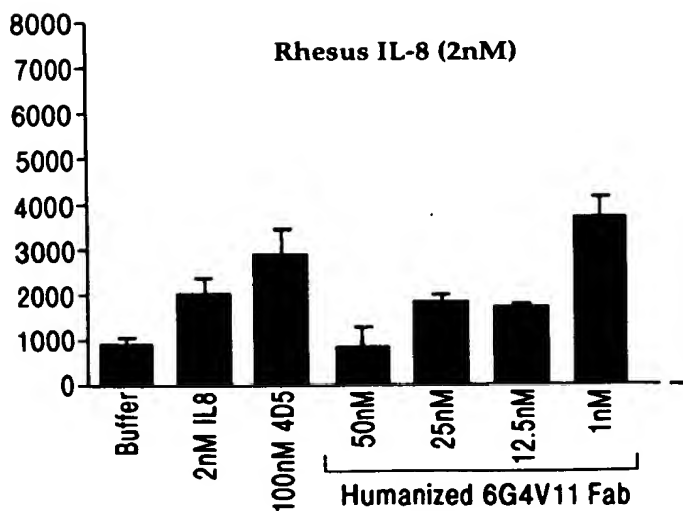


FIG. 30C

IC₅₀~22nM



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISLQPEDFATYYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLVGVYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGSGSGDFDYEKMANANKAMTENADENALQSDAKGLDSVATDYGAIDGFIGDVS
GLANGNGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLPQLPQSVECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMVVFSTFANILRNKES (SEQ ID NO.53)

FIG. 31A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

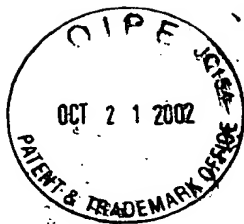
Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y
181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A
421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V
481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T
601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.51)

(SEQ ID NO.54)

FIG. 31B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISSLQPEDFATVYCSQST
HVPLTFFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMH
WVKQAPGKGLEWVGVIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.55)

FIG. 31C

FIG. 32

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





10/21/02

ANTIBODY FRAGMENT-OLIGOMER CONJUGATES AND FORMULATIONS

ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



FIG. 32



10/21/02

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 32





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

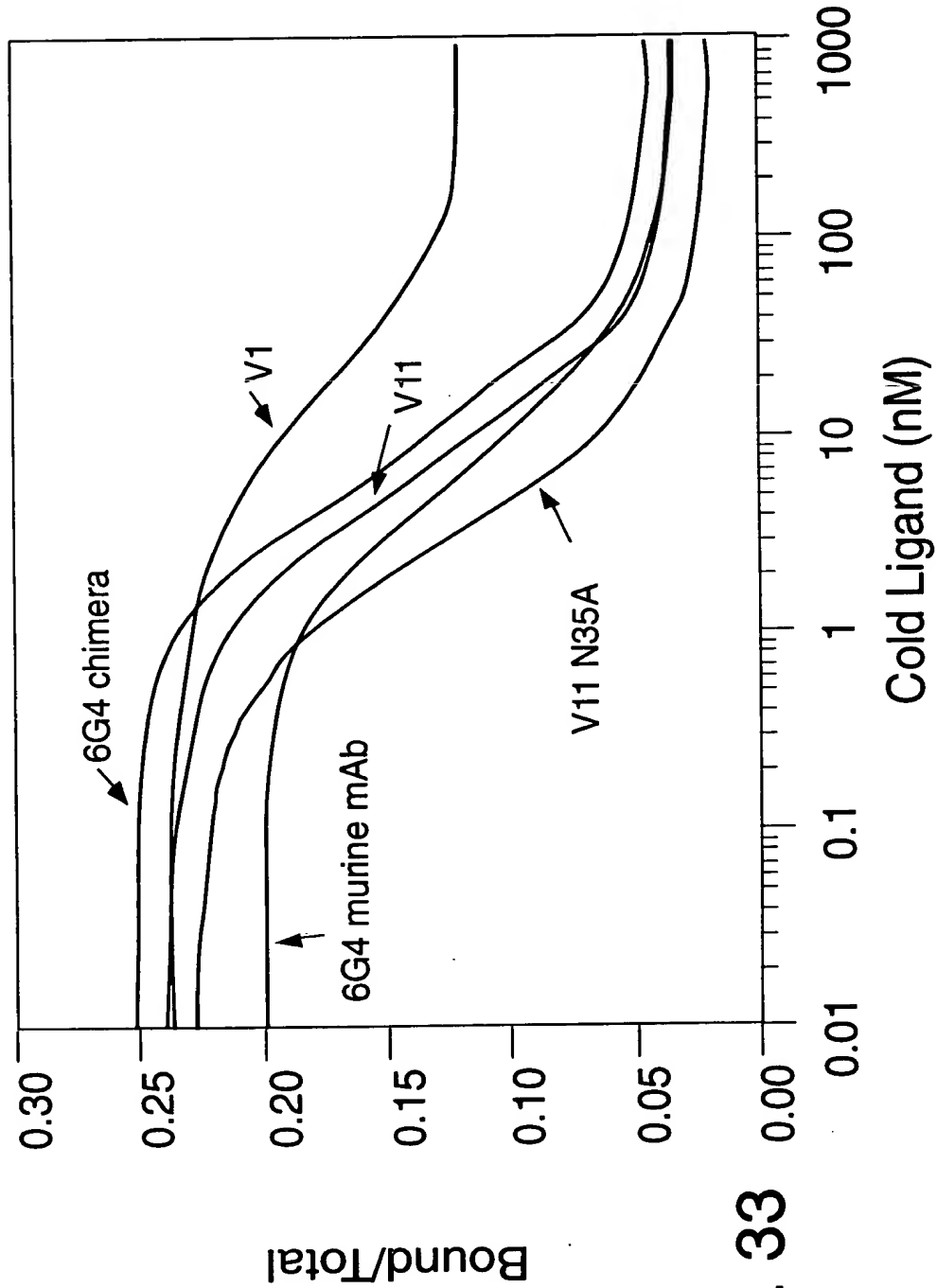
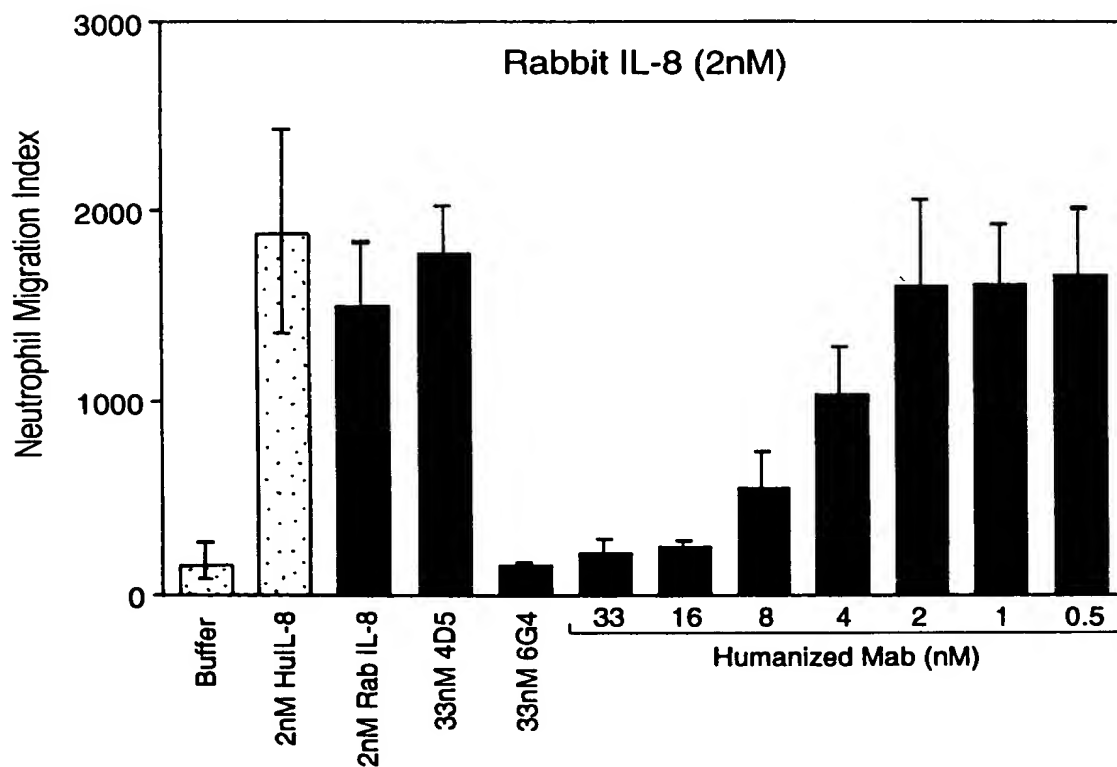
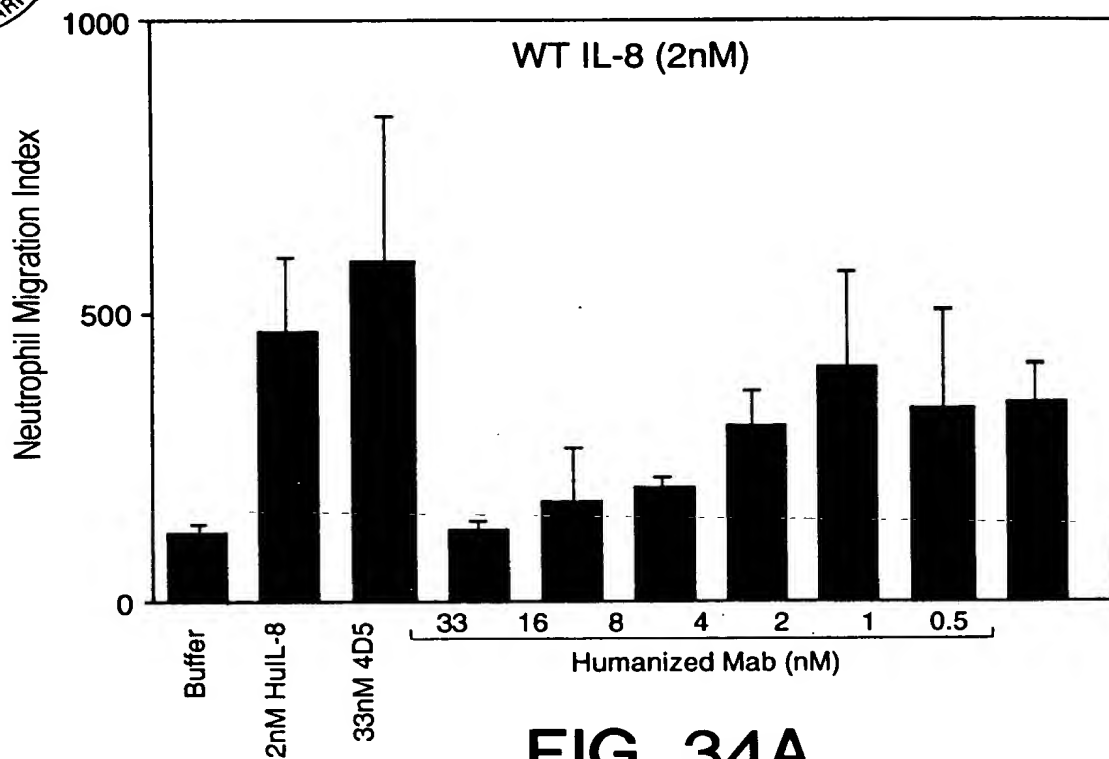


FIG. 33



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES
Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

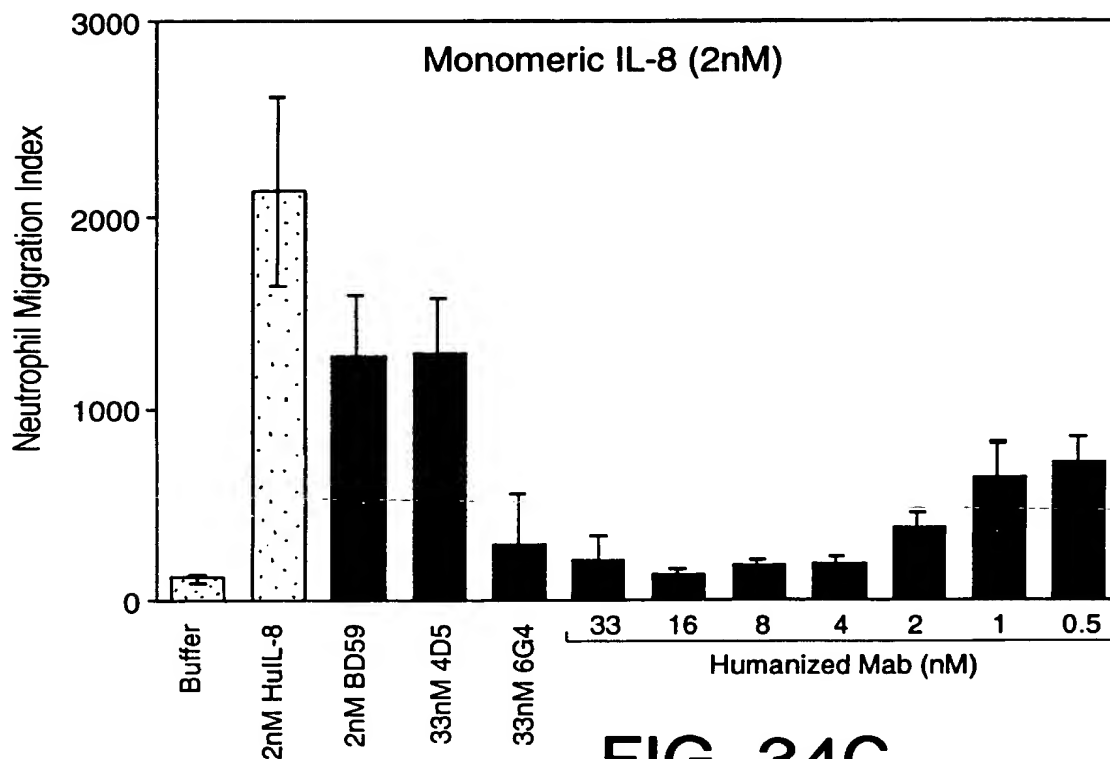


FIG. 34C

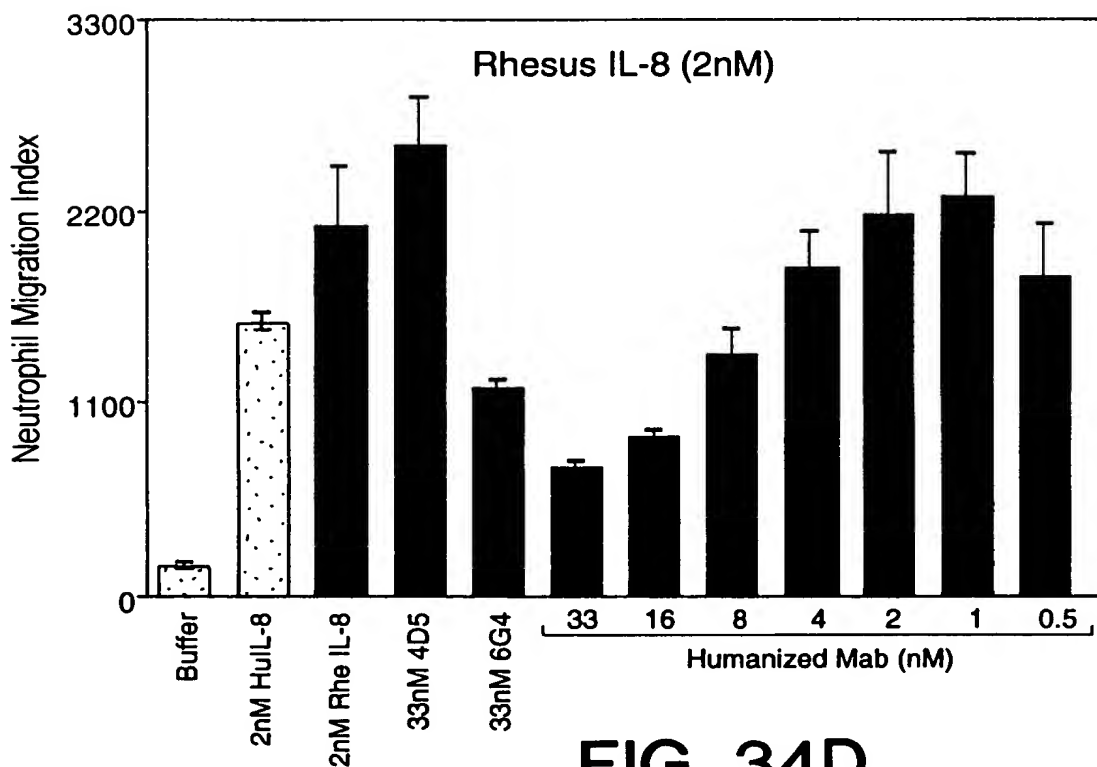


FIG. 34D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFGVPSRFGSGGTDFTLTISLSQPEDFATYYCSQST
HVPLTFFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGVIDPSNGETTYNQFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFDFVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHPKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGGER (SEQ ID NO.57)

FIG. 35



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G A T Y
181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A
421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V
481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T
601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
(SEQ ID NO.58)
721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCAG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.56)

FIG. 36



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTCTG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCC CCGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACCTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCTTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTCTG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTGCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTCTG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTCTGAT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

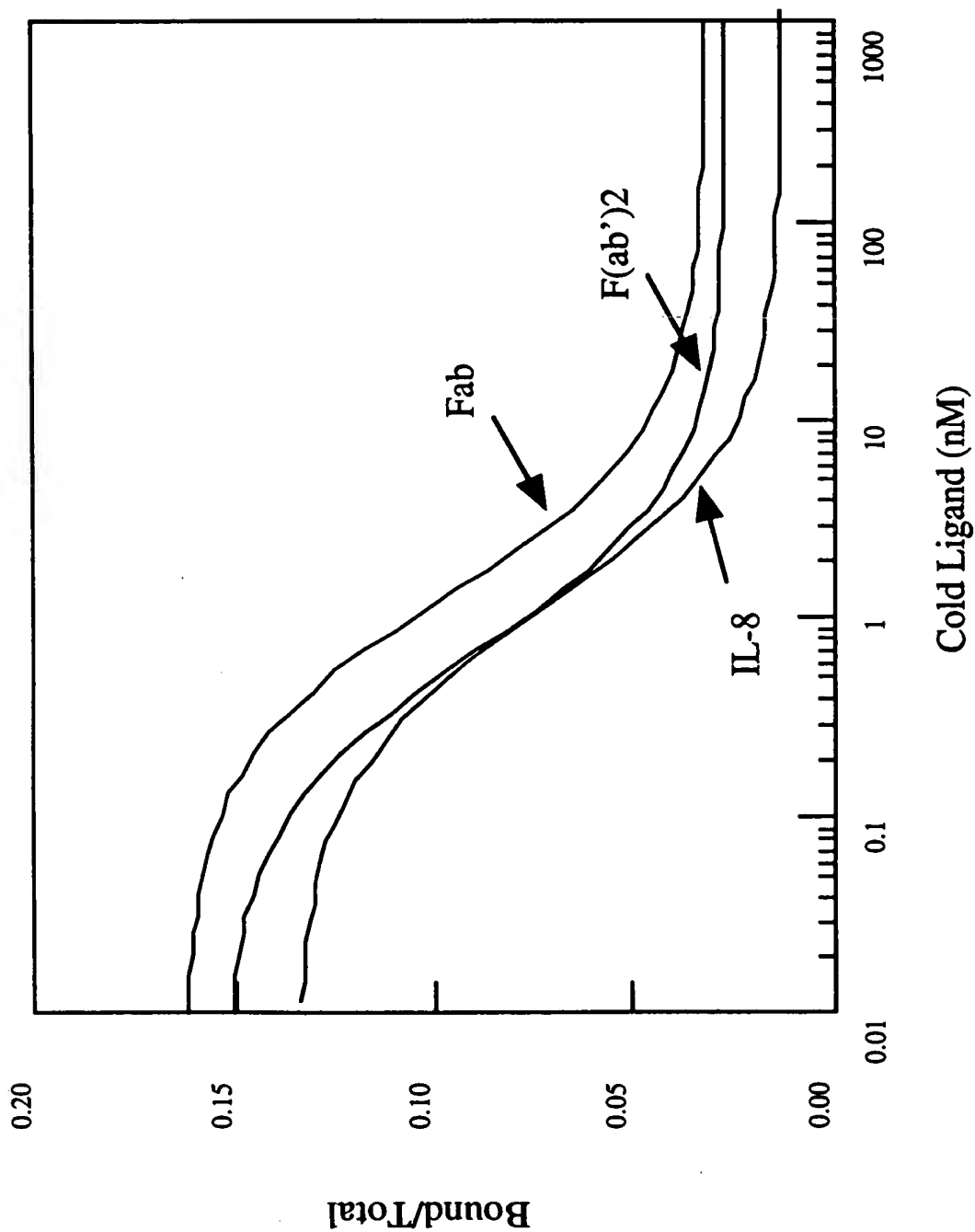


FIG. 38

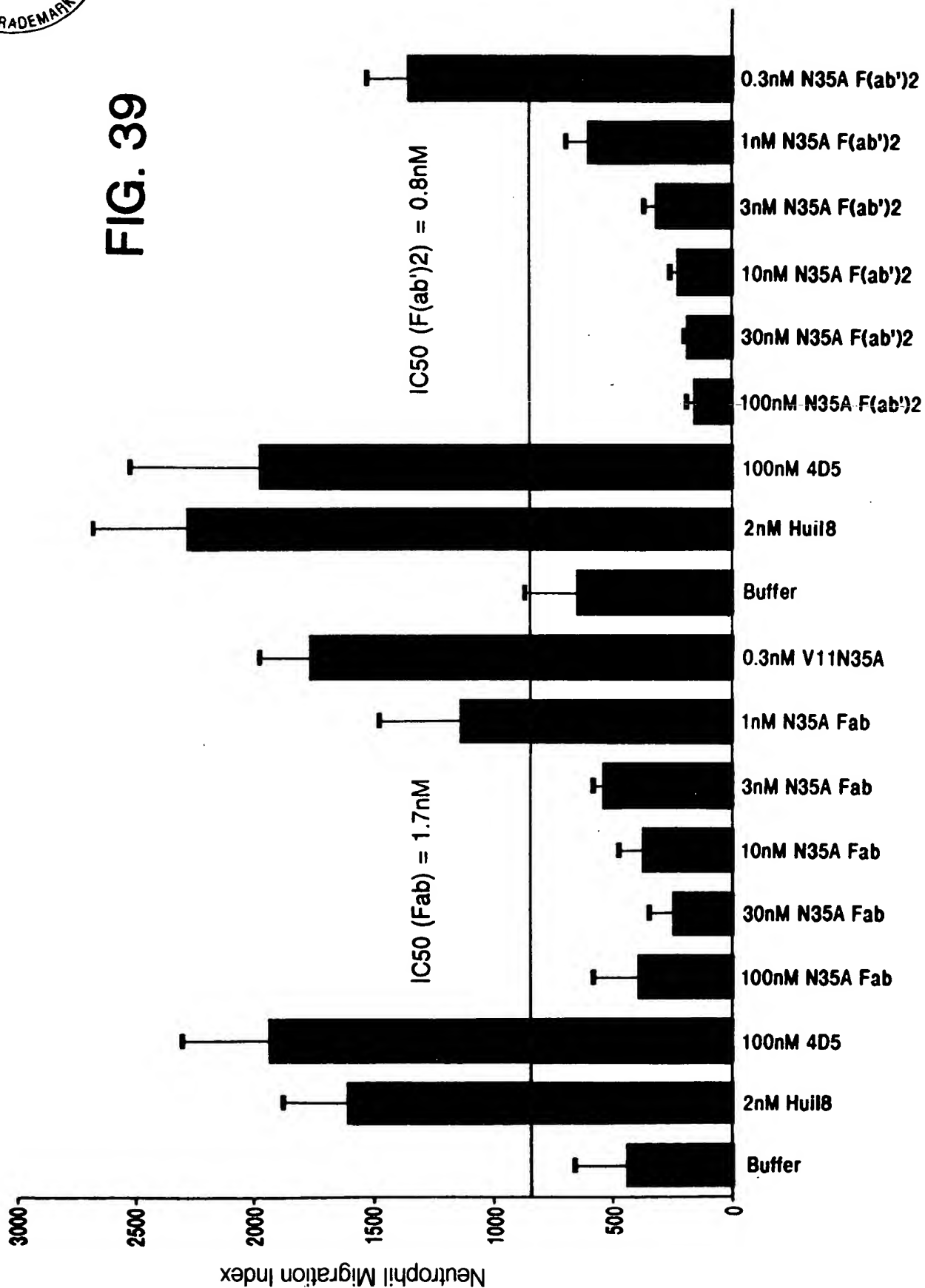


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 39



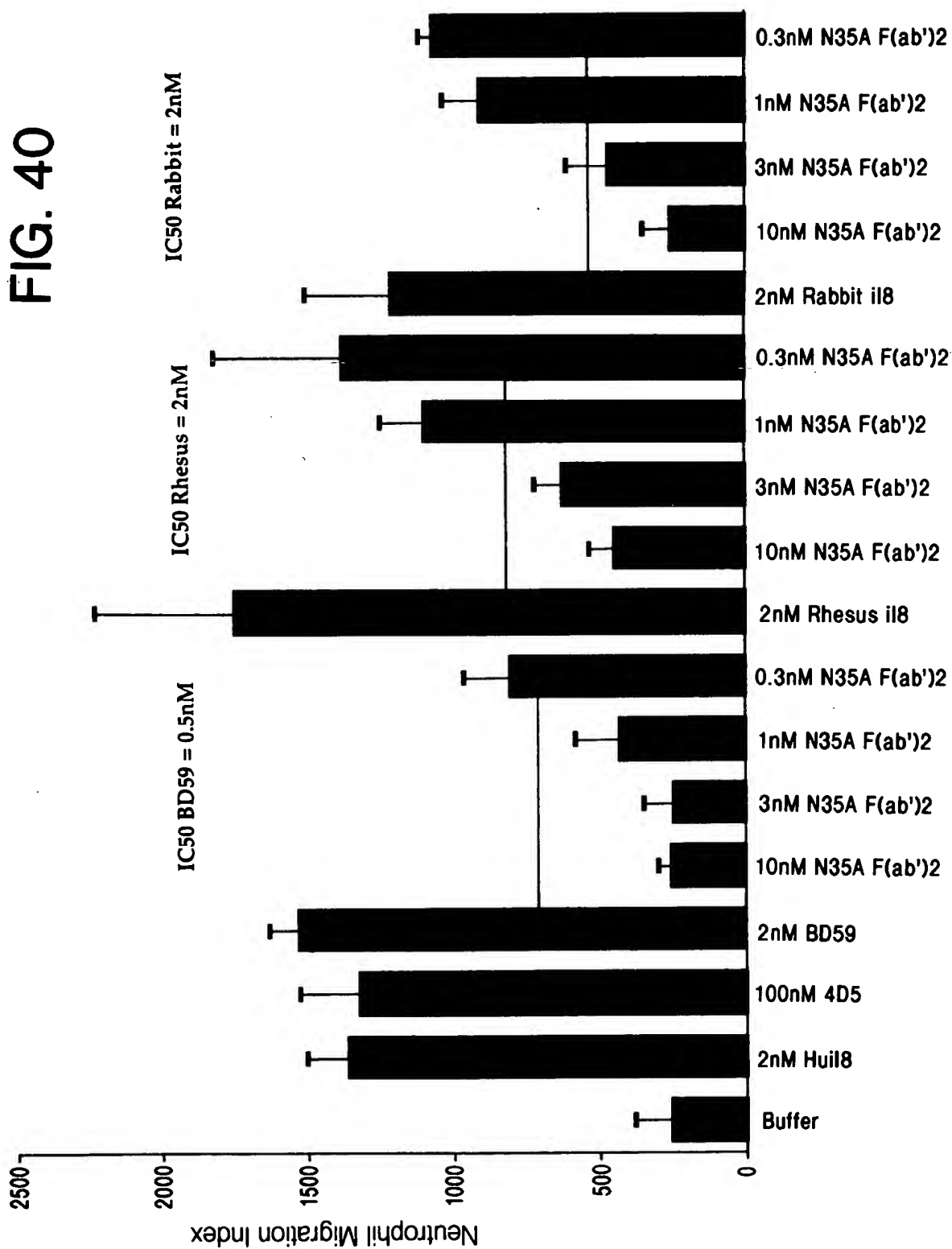


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 40



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



ecoRI pflMI pleI
apoI bslI mboII taqI
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTAT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAC AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA
bspMI sau3AI
hinPI hinPI mboI/ndeII[dam-]
hhai/cfoI hhai/cfoI dpnI[dam+]
mstI aluI dpnII[dam-]
avIII/fspI hindIII aciI
101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACCG GTTGATTGAT CAGGTACAGG
CTTGACACAC GGTCCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC GCGGTTTTAC TGGTTGTCG CAACTAACTA GTCCATCTCC
thai
fnuDII/mvni
fnu4HI
bsoFI
bbvI
fnu4HI bstUI snaBI
bsoFI bsh1236I
bbvI hinPI bsaAI
aluI hhai/cfoI
201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAACCATC CTCGTCAGTA
CCCCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACCTCGTAG GAGCACTCAT
maeII
cac8I
sfani bsmI
301 AAAAGTTAAT CTTTTCACA GCTGTCTATAA AGTTGTACAG GCGGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTTAACTA GAATTCGAGC
TTTTCATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAATATACAT AACATTGAT CTTAAGCTCG
haeIII/palI
mcrI
eagI/xmaIII/ec1XI
eaeI
cfrI
bsiEI ahdI/eam1105I
maeIII bsmAI
tru9I aluI
mseI pvuII
nspBII
tru9I mseI maeIII apoI banII
mseI bfaI taqI
ecoRI bsp1286
rmaI bsiHKAI
maeI bmyI
hgiJII
hgiAI/aspHI
ec1136II

FIG. 41A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
scrFI  
ncII  
mspI  
hpaII  
dsav  
xmaI/pspAI  
smaI  
scrFI  
ncII  
dsav  
cauII  
bsaJI  
avaI  
sau3AI taqI  
mboI/ndeII[dam-]  
rsal  
csp6I  
nlaIV  
kpnI cauII dpnII[dam-]  
hgiCI  
bani bsaJI alwI[dam-]  
asp718 bamHI avai  
acc65I alwI[dam-] mnlI  
mboII sfaNI  
501 TCGGTACCCG GGATCCTCT CGAGGTGAG GTGATTTAT GAAAAGAAT ATCGCATTC TTCTGCATC TATGTCGTT TTTTCTATTG CTACAAACGC  
AGCCATGGGC CCTAGGAGA GTCCCACTC CACTAAATA CTTTCTTA TAGCGTAAAG AAGAAGTAG ATACAGCAA AAAAGATAAC GATGTTGCG  
M K K N I A F L L A S M F V F S I A T N A  
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^  
-23  
sstI  
sacI  
hgiJII  
hgiAI/aspHI  
ecII36II  
bsp1286  
bsiHKAI  
bsmFI bmyI  
bsrI avai aluI  
tthIII/aspI banII aciI  
ecorV tthIII/aspI banII aciI  
501 ATACGTGAT ATCCAGATGA CCCAGTCCC GAGTCCCCTG TCCGCCTCTG TGGGGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT  
TATGGACTA TAGTCTACT GGGTCAGGG CTCGAGGGAC AGGCGGAGAC ACCCGCTATC CCAGTGGTAG TGGAGTCCA GTTCAGTTTC GAATCATGTA  
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H  
bspMI  
scfI  
psti  
sse8387I  
hphI maelII bspMI  
bsteII hphI bsgI  
hindIII csp6I  
dclI  
alul  
ndeIII  
rsal
```

FIG. 41B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

        scfFI      mval      ecORI      dsav      bstNI      aluI      bsrI      tfII      hinFI      bsmFI      taqI      bpmI/gsuI[dcM-]      pleI      clai/bsp106      bspDI[dam-]      hinFI
        601 GGTATAGGTG CTACGTATTT ACACCTGGTAT CAACAGAAAC CAGGAAAGC TCCGAAACVA CTGATTTCAC AAGTATCCAA TCGATTCTCT GGAGTCCCTT
          CCATATCCAC GATGCATAAA GTTGCTTTTG GTCTCTTTTCG AGGCTTTGAT GACTAAATGT TTCATAGGTT AGCTAAGAGA CCTCAGGGAA
          32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

        mspI      hpaII      bslI      bsaWI      sau3AI      mboI/ndeII[dam-]      dpuI[dam+]      dpuII[dam-]      alwI[dam-]      nlaIV      bstYI/xhoII      bamHI      alwI[dam-]      bsmFI
        701 CTGCTTCTC TGATCCGGT TCTGGGACGG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTCAC AGAGTACTCA
          GAGCGAAGAG ACCTAGGCCA AGACCTTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA CGGTTGAATA ATGACAAGTG TCTCATGAGT
          66 R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C S Q S T H

        styI      bsaJI      rsaI      csp6I      nlaIV      kpnI      hgiCI      banI      asp718      acc65I      maeII      bsmFI      acil      bsrBI
        801 TGTCCCGCTC ACGTTTGGAC AGGTATACCA GGTGGAGATC AAACGAACTG TGGCTGCACC ATCTGTCTTC ATCTTCCCGC CATCTGATGA GCAGTTGAAA
          ACAGGGCGAG TGCAAACTG TCCATGGTT CCACCTCTAG TTGCTTGAC ACCGACGTCG TAGACAGAG TAGAAGGCGG GTAGACTACT CGTCACTTT
          99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

        mboI/ndeII[dam-]      fnu4HI      bsoFI      bbvI      bbsI      mboII      bpuAI      bbsI      rsaI      csp6I      scaI      nlaIII

```

FIG. 41C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

scrFI
nvaI
ecorII
daav
bstNI
bsaJI
mnII
bslI
maeIII apyI[dcn+]
maeIII apyI[dcn+]
201 TCTGGAAGTGT GTGCTGTGTTGT GTGCTGTGTTGT ATCCACAGAG GGCACAAAGTA CAGTGAAGG TGGATAACGC CCTCCAATCG GGTAACCTCC
AGACCTTGAC GAAGACAACA CACGGACGAC TATTTGAAGA TAGGGTCTCT CCGGTTTCAT GTGACCTTCC ACCTATTGCG GGAGGTTAGC CCATTGAGGG
132 S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q

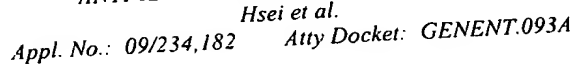
haeIII/palI
haeI
mnII
rsal
csp6I
fnu4HI
bsoFI
dclI
scFI
mnII
bbvI
hgaI
dclI
celII/espl
blpI/bpul102I
accI
cac8I
1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC
TCCTCTCACA GTGTCTGTC CTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC
166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

cac8I
aluI
sstI
sacI
hgiJII
hgiAI/aspHI
ecL136II
bsp1286
bsiHKAI
bmyI
haeIII/palI
sau96I
banII
asuI
dclI
hphI
eco0109I/draII
maeIII
aluNI[dcn-]
maeIII
accI
cac8I
1101 CTGCGAAGTC ACCCATCAGG GCCTGAGTCC GCGGCTCACA AAGAGCTTCA ACAGGGGAGA GTGTTAAGCT GATCTCTAC GCGGACGCA TCGTGGCCCT
GACGCTTCAG TGGGTAGTCC CGGACTCGAG CGGGCAGTGT TTCTCGAAGT TGTCCTCTCT CACATTCGA CTAGGAGATG CCGGCTGCGT AGCACCGGGA
199 C E V T H Q G L S S P V T K S F N R G E C O (SEQ ID NO.56)

maeIII
asp700
cac8I
asp700
xmnI
xmnI
haeIII/palI
haeI
mnII
rsal
csp6I
fnu4HI
bsoFI
dclI
scFI
mnII
bbvI
hgaI
dclI
celII/espl
blpI/bpul102I
accI
cac8I
1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC
TCCTCTCACA GTGTCTGTC CTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC GTGTGTTCC
166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

cac8I
aluI
sstI
sacI
hgiJII
hgiAI/aspHI
ecL136II
bsp1286
bsiHKAI
bmyI
haeIII/palI
sau96I
banII
asuI
dclI
hphI
eco0109I/draII
maeIII
aluNI[dcn-]
maeIII
accI
cac8I
1101 CTGCGAAGTC ACCCATCAGG GCCTGAGTCC GCGGCTCACA AAGAGCTTCA ACAGGGGAGA GTGTTAAGCT GATCTCTAC GCGGACGCA TCGTGGCCCT
GACGCTTCAG TGGGTAGTCC CGGACTCGAG CGGGCAGTGT TTCTCGAAGT TGTCCTCTCT CACATTCGA CTAGGAGATG CCGGCTGCGT AGCACCGGGA
199 C E V T H Q G L S S P V T K S F N R G E C O (SEQ ID NO.56)

FIG. 41D



```
scrFI
nciI
mspi
hpaiI
dsav
cauiI
bsli
xmai/pspai
smai
scrFI
nciI
dsav
cauiI
bsli
scrFI
mvai
ecoriI
```

FIG. 41E

[illegible]

FIG. 41E



1701 ATCGGTCTTC CCCCTGGCAC CCTCTCCAA GAGACCTCT GGGGGCACAG CGGCCCTGGG CTGCTGGTC AAGGACTACT TCCCGAACC GGTGACGGTG
 TAGCCAGAG GGGGACCGTG GGAGGAGTT CTCGTGGAGA CCCCCTGTC GCGGGACCC GACGGACCCAG TTCCTGATGA AGGGGCTTG CCACTGCCAC
 129 S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P V T V

 hinPI
 hhaI/cfoI
 nlaIV
 nari
 kasi
 hinII/acyI
 hgiCI
 haeII
 bani
 ddeI ahaII/bsaHI nspBII alw44I/snoI cauII scfI bsu36I/mstII/sauI mnlI bbvI bsteII bmyI bpmI/gsuI[dcM-]
 TCGTGGAACT CAGGCGCCT GACACGCGC GTGCACACCT TCCCGCTGT CCTACAGTCC TCAGGACTCT ACTCCCTCAG CAGCGTGGTG ACCGTGCCCT
 AGCACCTGA GTCCGGCGGA CTGGTCGCCG CACGTGTGGA AGGCGCGACA GGATGTCAGG AGTCCTGAGA TGAGGGAGTC GTCCGACCAC TGGCAGCGGA
 162 S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V T V P S

 aluI nlaIV
 fnu4HI hgiCI
 bsoFI bani
 bbvI bsp1286
 bstXI bmyI
 CCAGCAGCTT GGGCACCAG ACCTACATCT GCAACCTGAA TCACAAGCCC AGCAACACCA AGGTGACAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC
 GGTGTCGAA CCCGTGGTC TGGAGTAGA CGTGTGACTT AGTGTTCGG TCGTGTGGT TCCAGTGT TTTCAACT CTTTCACT GGGTTAGAA CACTGTTTG
 196 S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T

FIG. 41G

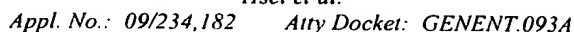


FIG. 41H

Hsei et al.

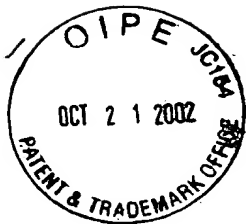
A circular black and white stamp. The outer ring contains the text "OIP E JC14" at the top and "PATENT & TRADEMARK OFFICE" at the bottom. In the center, the date "OCT 21 2002" is stamped.

FIG. 41I

[illegible]

FIG. 41J

acilI
 thaI
 fnuDII/mvnl
 bstUI nlaIII
 bsh1236I
 hinPI bcgI
 hhal/cfoI
 acilI
 fnu4HI
 bsoFI
 mboII
 bpuAI
 bbsI
 nlaIII
 nlaIV
 bsoFI
 hgiCI
 bbsI
 banI hpaII hhal/cfoI
 mnlI
 22901 TGGGGCGGG GCATGACTAT CGTCGCCGCA CTATGACTG TCTTCTTTAT CATGCAATC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG
 ACCCGGCCCC CGTACTGATA GCAGCGCGGT GAATACTGAC AGAAGAAATA GTACGTTGAC CATCCTGTCC ACGGCCGTCC CGAGACCCAG TAAAAGCCGC
 thaI
 fnuDII/mvnl
 bstUI
 bsh1236I
 hinPI
 hhal/cfoI
 bpnI/gsuI[dcM-]
 dpnII[dam-]
 dpnII[dam+]
 mboI/ndeII[dam-]
 haeIII/pali
 sau3AI
 sau96I
 avall
 asuI
 bsmFI
 33001 AGGACCGCTT TCCTGGAGC GCGACGATGA TCGGCTGTG GCTTGGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGCC TTCTCACTG GTCCCGCCAC
 TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCGGACAG CGAAGCCAT AAGCCTTAGA ACGTGGGGA ACGTGGGGA CAGGAGTGAC CAGGCGGCTG
 mcrI
 eagI/xmaIII/ecIXI
 eaeI
 hinPI
 cfrI
 hhal/cfoI
 bsiEI
 thaI
 fnu4HI
 fnuDII/mvnl
 bstUI
 cfr10I/bsrFI
 haeIII/pali
 hpaII
 bsoFI
 bsh1236I
 haeI
 acilI
 hgal
 bgII nlaIII haeIII/pali
 cac8I
 33101 CAACGTTTC GCGAGAGC AGGCCATTAT CGCGCGCATG GCGGCCGAGC CGCTTGGGTA CGTCTTGTG GCGTTCGCGA CGCAGGCTG GATGGCCTTC
 GTTTCGAAG CCGCTCTTCG TCCTGGTAATA GCGGCCGTAC GCGCGGTG GCGACCCGAT GCAGAACGAC CGAAGCGCT GCGTTCGAC CTACCGGAAG
 maeII
 psp1406I
 cac8I
 nruI
 bsh1236I
 foki haeIII/pali
 thaI fnuDII/mvnl
 fnuDII/mvnl
 bstUI
 bstUI
 bsh1236I
 mnlI
 haeI



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

        bspMI
        scrFI
        mvaI
        ecorII
        dsav
        thaI
        fnuDII/mvni
        bstUI
        cac8I
        haeI
        haeIII/palI
        bstNI
        fnu4HI
        bsoFI
        aciI
        mspI
        mslI
        sfaNI
        bsh1236I
        haeIII/palI
        bstNI
        hpaII
        sfaNI
        fokI
        aciI
        cac8I
        nlaIII
        apyI[dcn+]
        bsmFI
        aluI
        alwI[dam-]
3201 CCCATTATGA TTCTTCTCGC TTCCGGCGGC ATCGGGATGC CCGCGTTGCA GGCCATGCTG TCCAGGCAGG TAGATGACGA CCATCAGGGA CAGCTTCAAG
        GGGTAATACT AGAAGAGCGG AAGGCCCGCG TAGCCCTACG GGCGCAACGT CCGGTACGAC AGTCCGCTCC ATCTACTGCT GGTAGTCCCT GTCGAAGTTC
        fnu4HI
        bsoFI
        aciI
        mboII
        tfiI
        hinfi
        sau3AI
        bsh1236I
        mboI/ndeII[dam-]
        dpnI[dam+]
        dpnII[dam-]
        taqI[dam-]
        aciI
        dpnII[dam-]
        bglI
        cac8I
        nlaIII
        nlaII
3301 GATCGCTCGC GGCTCTTACC AGCCTAAGTTC CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTGGCATG
        CTAGCGAGCG CCGAGAATGG TCGGATGAA GCTAGTGACC TGGCGACTAG CAGTCCGCTC AAATACGGCG GAGCCGCTCG TGTACCTTGC CCAACCGTAC
        fnu4HI
        bsoFI
        hinPI
        hhaI/cfoI
        nlaIV
        narI
        kasI
        hinII/acyI
        hgiCI
        haeII
        banI
        aciI
        ahaII/bsaHI
        fnu4HI
        bsoFI
        aciI
        mspI
        hpaII
        nlaIV
        nael
        hgiCI
        cfr10I/bsrFI
        cac8I
        bani
        fnu4HI
        bsoFI
        aciI
        haeIII/palI
        sau96I
        scrFI
        nciI
        mspI
        hpaII
        dsav
        thaI
        fnuDII/mvni
        bstUI
        bsh1236I
        bsh1236I
        nlaIV
        asuI
        taqI
        mnlI
        aciI
        hgaI
        aciI
        nlaIII
        cauII
        mnlI
        CGCGGCCACC TCGACCTGAA TGAAGCCCG CGGCACCTCG
3401 GATTGTAGG CCGGCCCTAT ACCTTGTCTG CCTCCCGCG TTGCGTCGCG GTGCATGGAG CCGGCCCGCC GCGGCCGCTG AGCTGGACTT ACCTTCGGCC GCCGTGGAGC
        CTAACATCCG CCGCGGGGATA TGAACAGAC GGAGGGGCGC AACGCAGCGC CAGTACCTC GGCGCGGTGG AGCTGGACTT ACCTTCGGCC GCCGTGGAGC
```

FIG. 41L

[illegible]

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

sau3AI
mboI/ndelII[dam-]
mamI[dam-]
dpmI[dam+]
dpmII[dam-]
bstYI/xhoII
alwI[dam-]
mspI
hpaII
mroI bsabI[dam-] fnu4HI
bspMI
bspEI[dam-] bsoFI
bsaWI sfaNI bbvI
accIII[dam-] sfaNI
fokI cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
3801 TGGTCTTCGG TTTCCGTGTT TCGTAAAGTC TGGAAACGGC GAAGTCAGCG CCTGACCA mslI
ACCAAGCC AAAGGCACAA AGCATTTCAG ACCTTTGGC CTTCACTCGC GGGACGTGGT AATACAGGC CTAGACGTAG CGTCTACGA CGACCGATGG

          aciI
          bsmFI fokI
          sau96I sfaNI
          nlaIV aciI
          avall fnu4HI
          asuI bsoFI aciI mnlI
          ddel
          cac8I
          hinPI
          hhaI/cfoI
          tru9I haeII
          mseI eco47III
          ddel
          nspI
          scrFI
          nciI
          mspI
          hpaII
          bsrI
          bslI
          dsav nlaII
          maeII
          cauII
          psp1406I maeII nspHI
          pspl406I maeII nspHI nlaII apoI bslI
          CAACGTTCCA GTAACGGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCCTCTCT CGTTTCATCG GTATCAATTAC CCCCATGAAC AGAAATTCCC
4001 GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

```

FIG. 41N



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

4801 GAAACCCGAC AGGACTATAA AGATACCAGG CGTTTCCCCC TGAAGCTCC CTCGTGGCT CTCCTGTTCC GACCTGCGG CTTACCGGAT ACCTGTCCGC
CTTGGGCTG TCCTGATAAT TCTATGCTCC GCAAAGGGG ACCTTCGAGG GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA
bslI acil mspI fnu4HI hpaII bsaWI
scrFI mvaI ecoRII dsav bstNI apyI[dcM+] bsaJI aluI mnli hhaI/cfoI bssSI
hinPI
4901 CTTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATAGCTCA CGCTGTAGGT ATCTCAGTTC GGTGTAGGTC GTTCGGTCCA AGCTGGGCTG TGTGCACGAA
GAAAGAGGGA AGCCCTTCCG ACCGCGAAAG AGTATCGAGT GCGACATCCA TAGACTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC ACACGTGCTT
hinPI hhaI/cfoI haeII aluI scfI ddel
hgiAI/aspHI bsp1286 bsiHKAI bmyI apaLI/snoI alw44I/snoI
5001 CCCCCCGTTC AGCCCGACCG CTGGCGCTTA TCCGGTAACT ATCGTCTTGA GTCCAACCCG GTAAGACACG ACTTATCGCC ACTGGCAGCA GCCACTGGTA
GGGGGGCAAG TCGGGCTGGC GACGCGGAAT AGGCCATTGA TAGCAGAACT CAGGTGGGC CATTCTGTGC TGAATAGCGG TGACCGTCTG CCGTGACCAT
fnu4HI bsoFI nspBII acil hinPI mspI maeIII mcrI bbvI bsiEI hhaI/cfoI hpaII pleI hinfi cauII dsav nciI scrFI hpaII mspI alwNI[dcM-]
bsvI bsaWI
5101 ACAGGATTAG CAGAGCCAGG TATGTAGCGG GTGCTACAGA GTTCTTGAAG TGGTGGCCTA ACTACGGCTA CACTAGAAGG ACAGTATTG GTATCTGCGC
TGTCCTAATC GTCTCGCTCC ATACATCCGC CACGATGTCT CAAGAACTTC ACCACCGGAT TGATGCCGAT GTGATCTTCC TGTCAATAAC CATAGACGCG
mnli acil scfI haeIII/palI haeI bfaI rmaI maeI hinPI hhaI/cfoI

FIG. 41Q

Hsei et al.

[illegible]R141G⁺

5601 GGCCTTACCAT CTGGCCCCAG TCGTGCAATG ATACCGCGAG ACCCAGCGTC ACCGCTCCA GATTATCAG CAATAAACCA GCCAGCCGGA AGGCGCGAGC
CCGAATGGTA GACCGGGGTC ACGACGTTAC TATGGCGCTC TGGGTGGGAG TGGCGGAGGT CTAATAGTC GTTATTTGGT CGGTCCGGCT TCCCGGCTCG

bsrI fnu4HI fnuDII/mvni mspI hpaII bglI haeIII/pali haeIII/hinPI
sau96I nlaIV bsoFI haeIII/pali bsrDI aciI hphI nlaIV cfr10I/bsrFI cac8I asuI hhaI/cfoI
sau96I bsrI mnlI aciI foki mnlI bsrI msei asei/asnI/vspI aluI bsrI msei tru9I msti psp1406I
avaII asuI

5701 GCAGAACTGG TCCTGCAACT TTATCCGCCT CCATCCAGTC TATTAATGT TGCCTGGGAG CTAGAGTAAG TAGTTGCCCA GTTAATAGTT TCGCGCAAGT
CGTCTTCACC AGGACGTTGA AATAGCGGGA GGTAGGTCAG ATAATTACCA ACGGCCCTTC GATCTCATTC ATCAAGCGGT CAATTATCAA ACGCGTTGCA

scfFI nciI mspI hpaII rmaI maeI dsav cauII bfaI tru9I msei bsrI msei
sau96I mnlI aciI foki mnlI bsrI msei asei/asnI/vspI aluI bsrI msei tru9I msti psp1406I
avaII asuI

5801 TGTGTGCCATT GCTGCGAGCA TCGTGGTGTC ACGCTCGTCG TTTGGTATGG CTTCAATCAG CTCGGGTCC CAAGCATCAA GCGGAGTTAC ATGATCCCCC
ACAAAGGTAA CGACGTCGGT AGCACACAG TCGGAGCAGC AAACCATACC GAAGTAGTC GAGGCCAAGG GTTGCTAGTT CCGCTCAATG TACTAGGGGG

bsrI fnu4HI fnuDII/mvni mspI hpaII bglI haeIII/pali haeIII/hinPI
sau96I nlaIV bsoFI haeIII/pali bsrDI aciI hphI nlaIV cfr10I/bsrFI cac8I asuI hhaI/cfoI
sau96I bsrI mnlI aciI foki mnlI bsrI msei asei/asnI/vspI aluI bsrI msei tru9I msti psp1406I
avaII asuI

5901 ATCTTGTCGA AAAAGCGGT TAGCTCCTTC GGTCTCCGA TCGTTGTGTC AAGTAAGTTG GCCGCACTGT TATCACTCAT GGTATGGCA GCACTGCATA
TACAACACGT TTTTTCGCCA ATCGAGGAAG CCAGGAGGCT AGCAACAGTC TTCATTCAAC CGGCGTCACA ATAGTGAGTA CCAATACCGT CGTGACGTAT

bsrI fnu4HI fnuDII/mvni mspI hpaII bglI haeIII/pali haeIII/hinPI
sau96I nlaIV bsoFI haeIII/pali bsrDI aciI hphI nlaIV cfr10I/bsrFI cac8I asuI hhaI/cfoI
sau96I bsrI mnlI aciI foki mnlI bsrI msei asei/asnI/vspI aluI bsrI msei tru9I msti psp1406I
avaII asuI

FIG. 41S



FIG. 41T



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

        hinPI
        thal
        fnuDII/mvnI
        bstUI
        bsh1236I
        aciI
        nlaIV hhaI/cfoI
        nlaIII
        rcaI
        bspHI aciI
        bsmAI bsrBI
        6401 TTGCTCATG ACCGGATACA TATTGTAATG TATTAGAAA AATAACAAA TAGGGTTCC GCGACATTT CCCCAGAAAG TGCCACCTGA CGTCTAAGAA
        AACAGAGTAC TGGCCTATGT ATAAACTTAC ATAAATCTTT TTATTGTGTT ATCCCAAGG CGCGTGTAAG GGGGCTTTTC ACGGTGGACT GCAGATTCTT
        maeII
        hinII/acyI
        ahaII/bsaHI
        aatII ddeI
        sau96I
        haeIII/palI
        asuI
        ecoO109I/draII
        mnlI
        bssSI
        nlaIII
        rcaI
        bspHI
        6501 ACCATTATTA TCATGACATT AACCTATATAA AATAGGCGTA TCACGAGGCC CTTCCTCTTT CAA (SEQ ID NO.61)
        TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTCTCCGG GAAAGCAGAA GTT
        mboII
        bpuAI
        bbsI
        nlaIII
        tru9I
        mseI
        bspHI
        rcaI
        bspHI
        bssSI
        mnlI
        ecoO109I/draII
        asuI
        haeIII/palI
        sau96I
        nlaIV hhaI/cfoI
        aciI
        bsh1236I
        bstUI
        fnuDII/mvnI
        thal
        hinPI
        aatII ddeI
        ahaII/bsaHI
        hinII/acyI
        maeII
```

FIG. 41U



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accII(TCCGGA): 3867[dam-]
aciI(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
see hinII
acyI 1307 4678
aflIII(ACRYGT): 1788
ageI(ACCGGT): 1645 1813 2616 2637 2751 3408 6107 6489
ahaII/bsaHI(GRCGYC): 5435 5454 6146
ahaII/draI(TTTAAA): 346 5566
ahdI/eam1105I(GACNNNNNGTC): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
aluI(AGCT): 2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(GTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcn-](CAGNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apaLI/snoI(GTGCAC): 1831 4494 4992 6238
apoI(RAATTY): 1 391 4093
apyI[dcn+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vsPI(ATTAAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
aspHI see hgiAI
aspi see tthIIII
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463

FIG. 41V



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42



Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

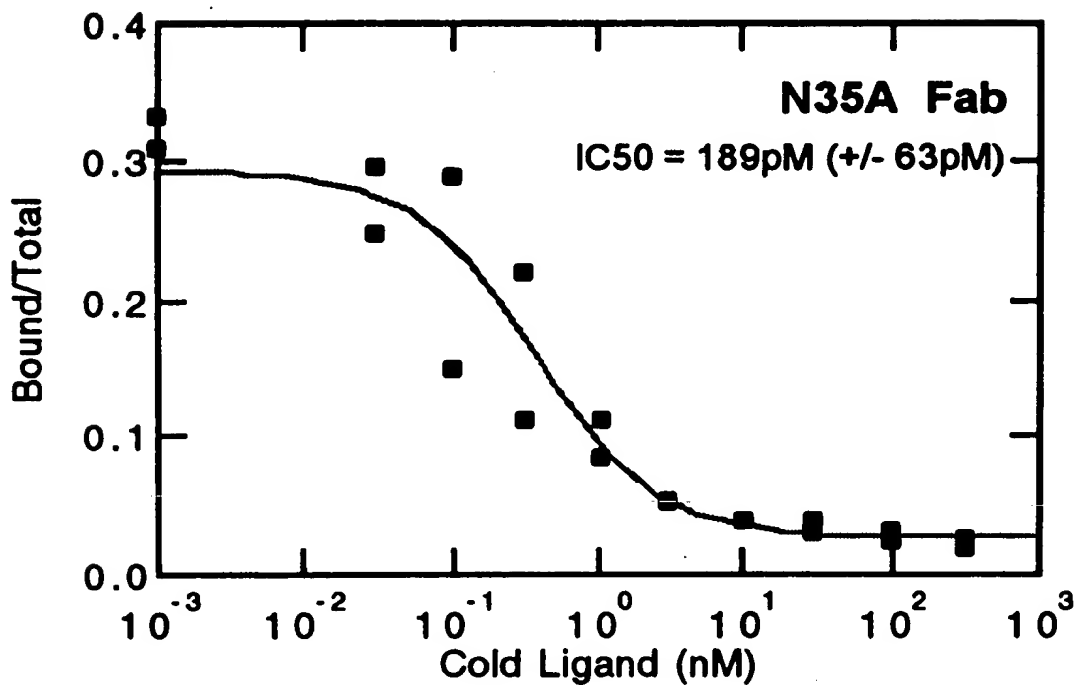


FIG. 43B

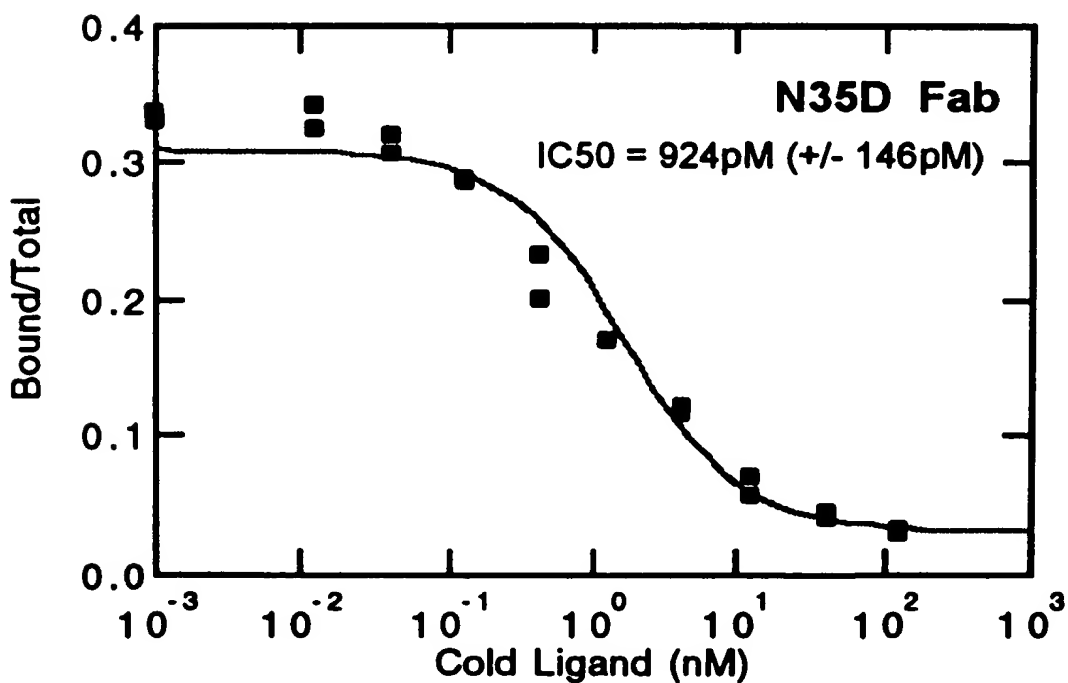


FIG. 43C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

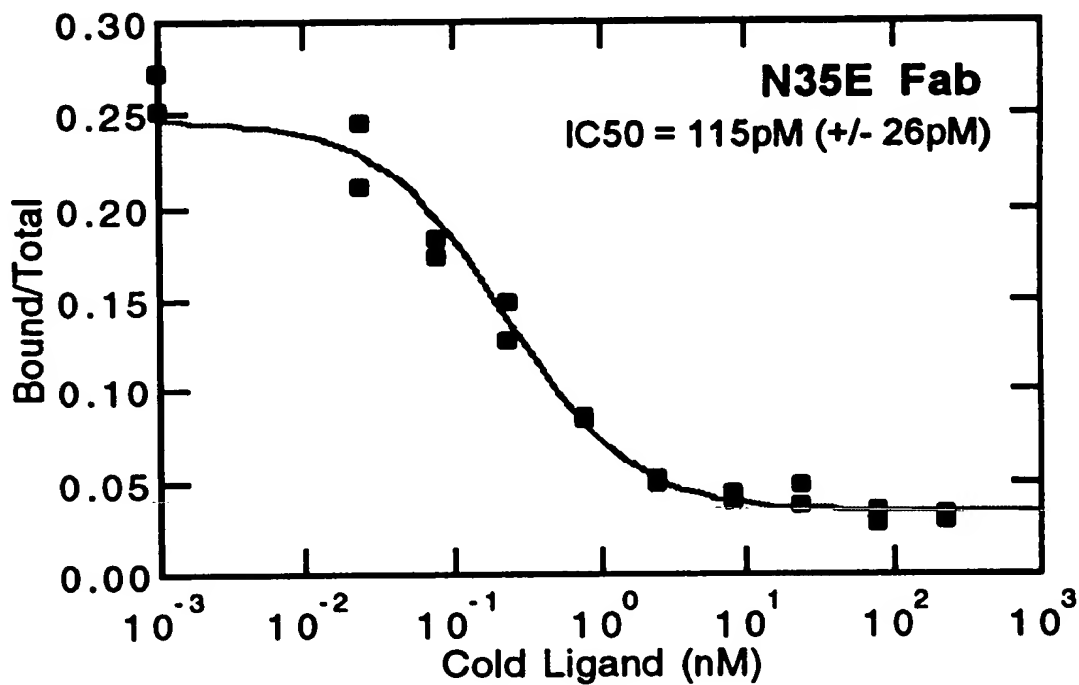


FIG. 43D

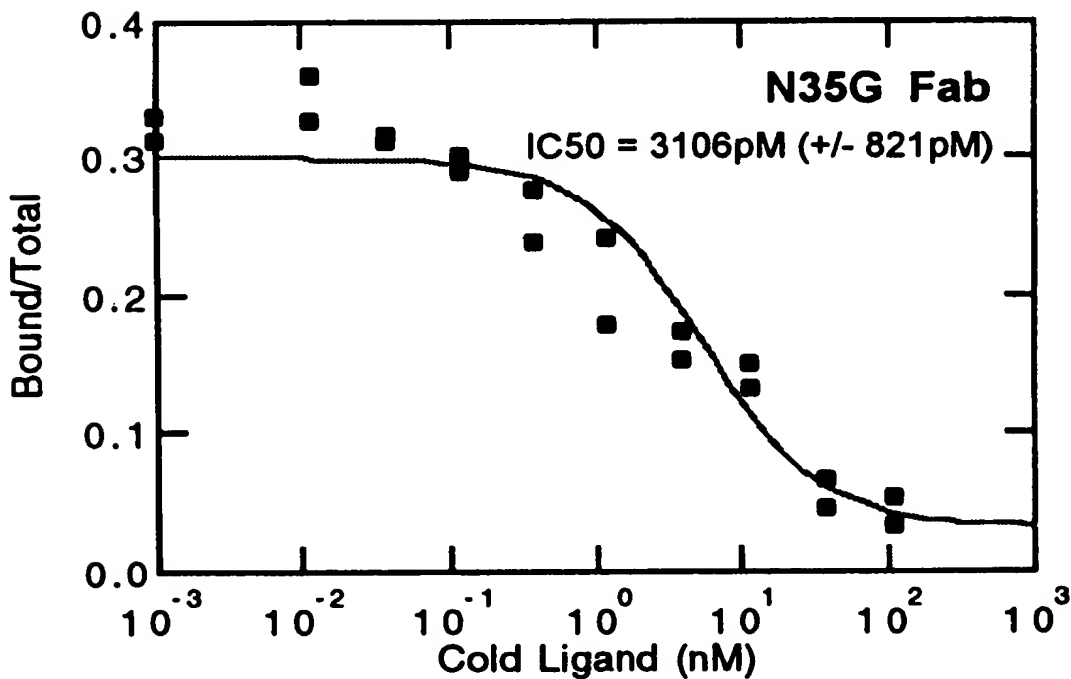


FIG. 43E

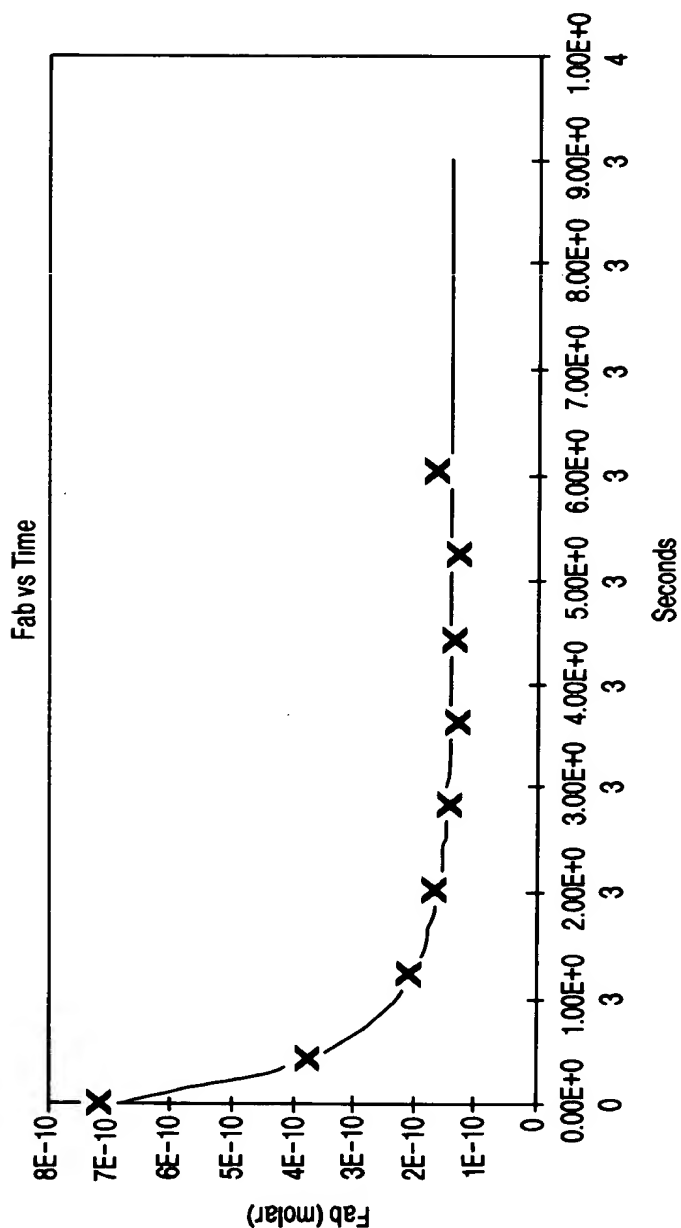


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S Q S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTT
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGCGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.62)

(SEQ ID NO.65)

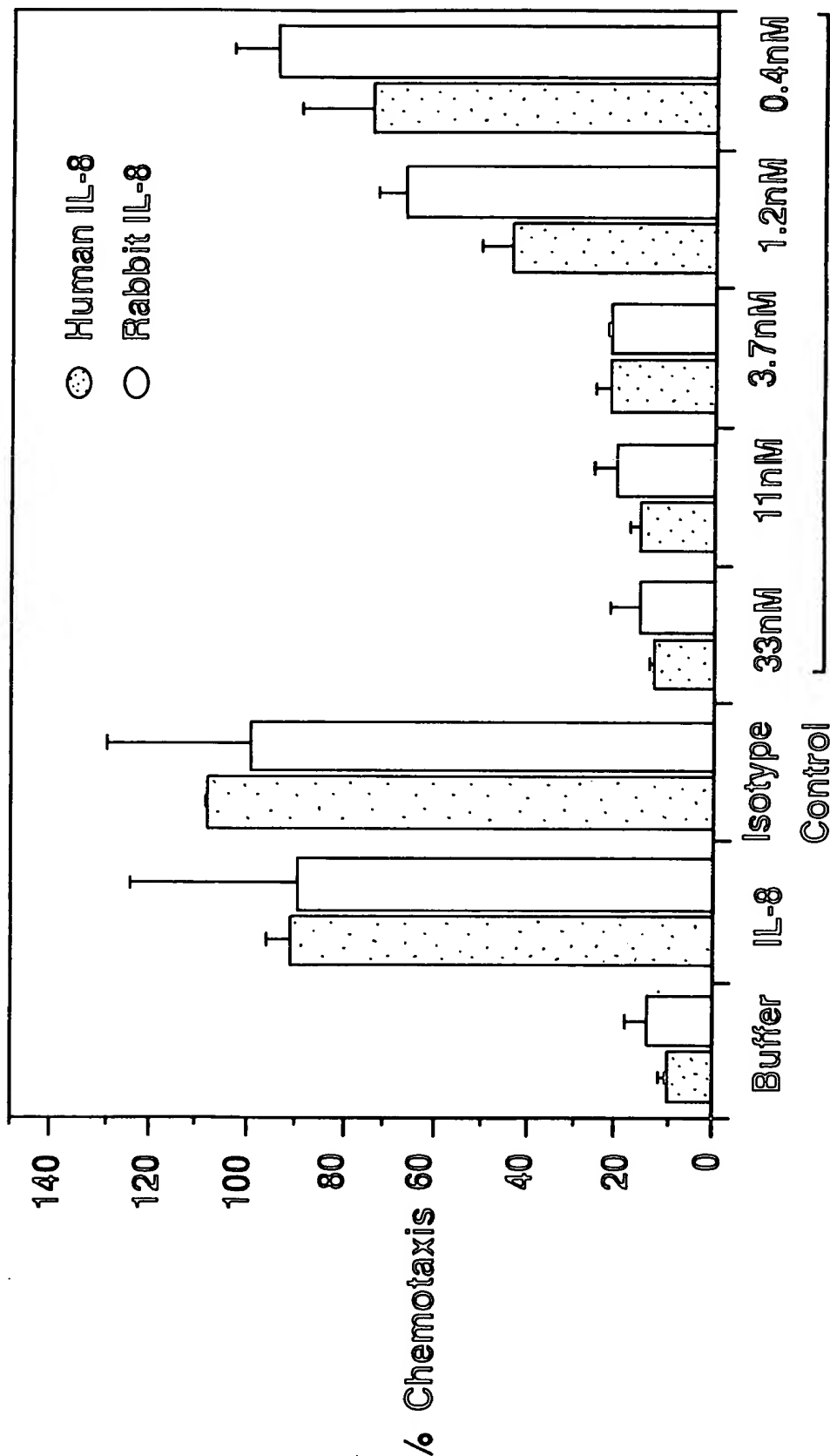
FIG. 45



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



Humanized
Anti-IL-8

FIG. 46



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

N35AH1upr

5'-CTAGTCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCCCTGTGCAGCTTCTGGCTACTCCTTC-3'
(SEQ ID NO.66)

N35AH1wr

5'-TCGAGAAGGAGTAGCCAGAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCGCCAGACTGCAC
AG-3' (SEQ ID NO.67)

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

```
> length: 8120 (circular)
>>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)
>>made from pSVI.WTSD.D by adding a linearization linker(LL) into the HpaI site
```

```

cac8I
aluI
sstI
sacI
hgiJII
hgiAI/asphi
ec136II
bsp1286
bsiHKAI
bmyI
banII
tagI
sau3AI aluI
mboI/ndeII(dam-)
dpnI(dam+)
pvuI/bspCI
pleI dpnII(dam-)
hinfi taqI(dam-)
rmaI mcrI pvuII
maeI bsiEI nspBII
bfaI taqI(dam-)
bsmFI nlaIV cac8I
1 TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGGTGTG GAATGTGTGT CAGTTAGGTT GTGGAAGTC CCCAGGCTCC CCAGCAGGCA
AAGCTCGAGC GGGCTGTAAC TAATAACTGA TCTCAGCTAG CTGTCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGGTCCGAGG GGTGCTCCGT
cac8I
sfanI
ppulOI
nsII/avaIII
nlaIII
sphi
nspi
nspHI
cac8I
scrFI
mvaI
ecorII
dsav
bstNI
apyI(dcm+)
bsaJI
nlaIV
cac8I
2 GAAGTATGCA AAGCATGTCAT CTCATTTACT CAGCAACCAG GTGTGGAAG TCCCGAGGCT CCCGAGCAGS CAGAAGTATG CAAGAGCATGC ATCTCAATTA
CTTCATACGT TTCGTACGTA GAGTTAATCA GTCTGTGGTC CACACCTTTC AGGGGTCCGA GGGGTGCTGC CTTCTCATAC GTTTCGTAGC TAGAGTTAAT
nlaIII
styI
ncoI
bslI dsal
aciI bsaJI
3 GTCAGCAACC ATAGTCCCGC CCCTAATCC GCCATCCCG CCCCTAATCT CGCCCATTTCT CCGCCCATCT CGTGACTAAT TTTTTTTTATT
TATCAGGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GGGGGTCAAG GCGGGTNAAG GCGGGGTGAC CCACTGATTA AAAAAAATA
CAGTGGTTGG

```

FIG. 48A

[illegible]

FIG. 48B

```

scrFI
mvaI
ecorII
dsav
bstNI
tfII
hinfI
mboII
apyl[dcmt+]
sexAI
ddei mboII taqI
ahaiII/drai
tru9I
msei

601 CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAGAAT CGACCTTTAA
GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTGTGCT TAGACCACCTA ATACCATCC TTTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAATTT

sstI
sacI
hgiII
hgiAI/aspHI
ecII36II
bsp1286
bsiHKAII
bmyI
mnli aluI
mnli aluI
bssSI banII
bsII bseRI
bstXI foki sfaNI msei
afII/bfRI
tru9I
msei
aseI/asnI/vspI
701 AGGACAGAAT TAATATAGTT CTCAGTAGAG AACTCAAGA ACCACCAGA GGAGCTCATTT TCTTTGCCAA AAGTTTGAT GATGCCITAA GACTTATTGA
TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGSTGGTGCT CCTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT

haeIII/palI
haeI

scrFI
mvaI
ecorII
dsav
bstNI
tfII
apyl[dcmt+]
hinfI
apyl[dcmt+]
hinfI
mnli
accI nlaIII
mnli
ddei pleI
hpaII
bsaWI
801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTITGGATA GTGGGAGCA GTTCTGTTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT
TGTTGGCCTT AACCGTTTCAT TTCTATCTGTA CCAACCTAT CAGCCTCCGT CAAGACAAAT GGTCTCTCGG TACTTAGTTG GTCCGGTGA ATCTGAGAAA

```

FIG. 48C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

          hgaI
          hinII/acyI
          ahaII/bsaHI
scrFI
mvaI      mnII
ecoRII
dsav
bstNI     ecoNI
          apyI[dam+] mnII
          bsaJI     bslI ddeI
          901 GTGACAAGGA TCATGCAGGA ATTTGAAAGT GACACGTTTT TCCCAGAAAT TGATTGGGG AAATATAAAC CTCTCCAGA ATACCCAGGC GTCTCTCTG
             CACTGTTCCT AGTACGTCCT TAAACTTTCA CTGTGCAAAA AGGTCITTTA ACTAAACCCC TTTATATTG GAGAGGTCT TATGGGTCCG CAGGAGAGAC
             maeIII alwI[dam-] apoI      maeIII
             maeII
             aflIII
             1001 AGTCCAGGA GGAAAAGGC ATCAAGTATA AGTTGAAGT CTACGAGAAG AAGACTAAC AGGAAGATGC TTTCAAGTTC TCTGCTCCCC TCCTAAAGCT
             TCCAGGTCCT CCTTTTCCG TAGTTCATAT TCAAACTTCA GATGCTTTC TTCTGATTG TCTTCTACG AAGTTCAAG AGACGAGGG AGGATTTTCA
             ^END DHR
             sfaNI
             mboII
             mboII
             aluI
             1101 ATGCATTTT ATAGACCAT GGGACTTTTG CTGCTTTAG ATCCCTTTG CTTCGTTAGA ACCGAGCTAC AATTAATACA TAACCTTATG TATCATACAC
             TACGTAAAA TATTCTGGTA CCTGTGGA CCCTGAAAAC GACCGAAATC TAGGGAACC GAAGCAATCT TGCCTGATG TTAATTATCT ATTGAATAC ATAGTATG
             sau96I
             avaiI
             styI
             bsaJI
             sau3AI
             mboI/ndeII[dam-]
             dpnI[dam+]
             dpnII[dam-]
             alwI[dam-]
             bstVI/xhoII
             cac8I
             ppulOI
             nslI/avaIII
             dsal bsmFI
             bsaJI
             aluI
             fnu4HI
             bsoFI
             bbyI
             asel/asnI/vspI
             msel
             tru9I
             sau96I
             avaiI
             asul
             scrFI
             mvaI
             ecoRII

```

FIG. 48D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACCTTTGCC TTCTCTCTCCA CAGGTGTCCA CACTGTGCACC TCCTGTTCTAT CGATGAATT
TATGCTAAAT CCACTGTGAT ATCTATTGTA GGTGAACCG AAGAGAGGT GTCCACAGGT GAGGTCCAG GTTACAGTGG AGCCAGATA GCTTAAGTAA
seq from pRK6G425VH: Cla-AvrII⁺

1301 CCACCATGGG ATGGTCATGT ATCATCCTTT TTCTAGTAGC AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TCTGGCGGTG GCCTGGTGCA
GGTGTGACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCTTCAACT CGATCAGTCC AGACCGCCAC CGGACCCAGT
E V Q L V Q S G G L V Q

1

1401 GCCAGGGGCG TCACTCCGTT TGTCCTGTGC AGCTTCTGCG TACTCCTTCT CGAGTCACTA TATGACTGG GTCCGTAGG CCCCCGGTAA GGGCCTGGAA
CGGTCCCCCG AGTGAGGCAG ACAGGACACG TCGAAGACCG ATGAGGAAGA GTCACTGAT ATACTGACC CAGGCAGTCC GGGGCCCATTT CCGGACCTT
14 P G G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

FIG. 48E

bslI
sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmII[dam-]
alwI[dam-] hphI
1501 TGGGTTGGAT ATATTGATCC TTCCAATGGT GAACTACCT ATATCAAAA GTTCRAGGCG CGTTTCACTT TATCTCGCGA CAATCCAAA AACACAGCAT
ACCAACCTA TATACTAGG AAGGTTACCA CTTTGATGGA TATTAGTTTT CAAGTTCCCG GCAAAGTCAG ATAGAGCGCT GTTGAGGTTT TTGTGTCCTA
47 W V G Y I D P S N G E T T Y N Q K F K G R F T L S R D N S K N T A Y
scfI
patI
bsgI
bspwI
cac8I ddeI drdI
cac8I mnlI
1601 ACCTGCAGAT GAACACCCTG CGTGCTGAGG ACACTGCCCT CTATTACTGT GCAAGAGGGG ATTATCGCTA CAATGGTGAC TGGTTCTTCG ACGTCTGGGG
TGGACGTCTA CTTGTGGGAC GCACGACTCC TGTGACGGCA GATAATGACA CGTTCTCCCG TAATAGCGAT GTTACCACATG ACCAAGAAGC TGCAGACCCC
81 L Q M N S L R A E D T A V Y Y C A R G D Y R Y N G D W F F D V W G
sau96I
sau96I
nlaIV
hgiJII
bsp1286
esp3I
bspl20I
bsmBI
scfI
mvaI
ecorII
dsav
betNI hphI
apyI[dcm+]
bsaJI maeIII
bseRI mnlI
bsteII bsmAI
nlaIV
1701 TCAAGGAACC CTGCTACCGC TCTCTCTGGC CTTCCACCAAG GGGCCATCGG TCTTCCCTCC TCCACGAGCA bsaJI mnlI bmyI nspBII apyI[dcm+]
AGTTCCCTTG GACCACTGGC AGAGGAGCG GAGGTGGTTC CGGCTAGCC AGAAGGGGGA CGGTGGGAGG AGGTTCTCGT GGAGACCCCC GTGTGCGCG
114 Q G T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A
thai
fnuDI/mvnI
bstUI
bsh1236I
nrui
haeIII/pali
sau96I
asuI
hphI
mboII maeII
hphI
mboII maeII
bsrI
maeIII
taqI
hinII/acyI
ahaiI/bsaHI
aatII
bsrI
maeIII
taqI
bsaJI
sau96I
haeIII/pali
asuI
fnu4HI
bsoFI
bsp1286 acII bsaJI
bsiHKA
bmyI mnlI
bmyI mnlI
TCCACGAGCA
CGTCTGGGG
CACAGCGGCC
AGGTTCTCGT
GGAGACCCCC
GTGTGCGCG

FIG. 48F

[illegible]

FIG. 48G

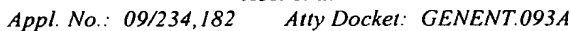


FIG. 48H



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
scrFI nciI mspI hpaII dsav caulI xmaI/pspAI  
smal scrFI nciI dsav caulI foki  
bsaI bsaJI mboII earI/ksp632I  
bspl407I/bsrGI bslI bslI avai  
avaI  
2401 CAGCCCCGAG AACACACAGG GTACACCCCTG CCCCACATCCC GGAAGAGAT GACCAAGATC CAGGTACGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA  
GTCCGGGCTC TTGGTGTCCA CATGTGGGAC GGGGTAGGG CCCTTCTCTA CTGTTCTTG GTCCAGTCGG ACTGGACGGA CCAGTTTCCG AAGATAGGTT  
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S  
rsal csp6I bslI bsaJI mboII earI/ksp632I  
bspl407I/bsrGI bslI bslI avai  
avaI  
2401 CAGCCCCGAG AACACACAGG GTACACCCCTG CCCCACATCCC GGAAGAGAT GACCAAGATC CAGGTACGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA  
GTCCGGGCTC TTGGTGTCCA CATGTGGGAC GGGGTAGGG CCCTTCTCTA CTGTTCTTG GTCCAGTCGG ACTGGACGGA CCAGTTTCCG AAGATAGGTT  
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S  
mspI hpaII  
fnu4HI bsoFI bsvI  
bsrDI bsvI  
mslI bsaJI  
2501 GCAGATCGC CGTGGAGTGG GAGAGCAATG GAGAGCGGA GAACAACATC AAGACCAGC CTCCCGTGCT GGACTCCGAC GGCTCCTTCT TCCTCTACAG  
CGTGTAGCG GCACCTCACC CTCTCGTTAC CCGTCGCTC CTGTGCTG TTTCTGTGATG TTCTGTGCG GAGGGCAGCA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC  
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F L Y S  
pleI hinfI nlaIV mboII scfI cac8I  
mnlI  
mboII  
bpuAI maelI xmnI bbsI nlaIII sfanI mnlI  
fnu4HI bsoFI bsvI bspMI bsvI asp700 nlaIII  
2601 CAAGCTCACC GTGGACAAGA GCAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC ACTACAGCA GAAGAGCCTC  
GTTGAGTGG CACCTGTCT CGTCCACCGT CGTCCCTTG CAGAAGATGA CGAGGCACTA CGTACTCCGA GACGTGTTGG TGATGTGCGT CTTCTCGGAG  
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L  
sapI mboII mnlI earI/ksp632I
```

FIG. 48I



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

```

sau96I      sau96I      sau96I      sau96I      sau96I      sau96I      sau96I      sau96I      sau96I      sau96I
acII      haeIII/palI      acII      haeIII/palI      acII      haeIII/palI      acII      haeIII/palI      acII      haeIII/palI
fnu4HI      asuI      fnu4HI      asuI      fnu4HI      asuI      fnu4HI      asuI      fnu4HI      asuI
bsoFI      nlaIII      bsoFI      nlaIII      bsoFI      nlaIII      bsoFI      nlaIII      bsoFI      nlaIII
sfII      styI      sfII      styI      sfII      styI      sfII      styI      sfII      styI
eaeI      ncoI      eaeI      ncoI      eaeI      ncoI      eaeI      ncoI      eaeI      ncoI
cfri      dsal      cfri      dsal      cfri      dsal      cfri      dsal      cfri      dsal
aluI      haeIII/palI      aluI      haeIII/palI      aluI      haeIII/palI      aluI      haeIII/palI      aluI      haeIII/palI
hindIII      bglI      bsaJI      hindIII      bglI      bsaJI      hindIII      bglI      bsaJI      hindIII      bglI      bsaJI
bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI
bsmAI      cauII      bsmAI      cauII      bsmAI      cauII      bsmAI      cauII      bsmAI      cauII      bsmAI      cauII
baII      cauII      baII      cauII      baII      cauII      baII      cauII      baII      cauII      baII      cauII
2701      TCCCTGTCTC      CGGGTAAATG      AGTCCGACGG      CCCTAGAGTC      GACCTGCAGA      AGCTTGCCG      CCATGGCCCA      ACTTGTTTAT      TGCAGCTTAT      AATGGTTTAC
AGGCACAGAG      GCCCATTTAC      TCACGCTGCC      GGGATCTCAG      CTGGACGTCT      TCGAACCCGC      GGTACCCGGT      TGAACAAATA      ACGTCGAATA      TTACCAATGT
447      S      L      S      P      G      K      O      (SEQ ID NO.71)

sfanI      apoI      sfanI      apoI      sfanI      apoI      sfanI      apoI      sfanI      apoI      sfanI      apoI      sfanI      apoI      sfanI      apoI
2801      AATAAGCAA      TAGCATCACA      AATTTCACAA      ATAAAGCATT      TTTTCACTG      CATTCTAGTT      GTGGTTGTC      CAAACTCATC      AATGATCTTT      ATCATGTCTG
TTATTTCGTT      ATCGTAGTGT      TTAAAGTGTT      TATTTCGTAA      AAAAGTGAC      GTAAGATCAA      CACCAACAG      GTTGAGTAG      TTACATAGAA      TAGTACAGAC
nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)      nlaIII      alwI(dam-)

sau3AI      mboI/ndeII(dam-)      dpnI(dam+)      dpnII(dam-)      pvuI/bspCI      mcrI      bsiEI      taqI(dam-)      tru9I      claI/bspI06(dam-)      bspDI(dam-)      maeI      sau3AI      xmnI      mboI/ndeII(dam-)      dpnI(dam+)      asp700      dpnII(dam-)      asel/asnI/vspI      bsaJI      hhaI/cfoI      nlaIII      fnu4HI      haeI      bsoFI      styI      bbvI      ncoI      hinPI      dsal      haeIII/palI
2901      GATCGATCGG      GAATTAATTC      GCGCAGCAC      CATGGCCTGA      AATAACCTCT      GAAAGAGGAA      CTTGGTTAGG      TACCTTCTGA      GCGGAAAGA      ACCATCTCTG
CTAGCTAGCC      CTTAATTAG      CGCGTCTG      GTACGGACT      TTATTGGAGA      CTTTCTCCTT      GAACCAATCC      ATGGAAGACT      CCGCCTTCT      TGGTAGACAC
rsal      csp6I      nlaIV      kpnI      hgiCI      bani      asp718      mnII      acc65I      ddel      acII
```

FIG. 48J

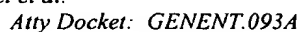


FIG. 48K

[illegible]

FIG. 48L



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

sau96I
avaII
asuI
scrFI
mvaI
ecoriI
dsav
bstNI
apyI[dcM+]
bslI bsaJI
3501 CCACCTTTTC TTTTCTCCA CAGGTGTCCA CTCACAGGTC CAACTGCACC TGGGTTCCGC AAGCTAGCTT GGGCTGCATC GATTGAATTC CACCATGGGA
GGTGAAAAAG AAAAAGAGGT GTCCACAGGT GAGGTCCAG GTTGACGTGG AGCCAAGCGC TTGCATCGAA CCCGACGTAG CTAACCTAAG GTGGTACCTT
^cloning linker

nlaIII
maI
maeI
thaI nheI
fnuDII/mvni
mnli
bsaJI nruI aluI
bsmFI bmyI
rsal
bpml/gsuI[dcM-]
bsrI csp6I
actGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCGCAGCTC CCTGTCCGC TCTGTGGCG
3601 TGGTCATGTA TCATCCTTTT TCTAGTAGCA
ACCAGTACAT AGTAGGAAA AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGCTCGAG GGACAGCGG AGACACCCGC
1
nlaIII foki
bsrI csp6I
actGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCGCAGCTC CCTGTCCGC TCTGTGGCG
D I Q M T Q S P S S L S A S V G D

maeIII hphI bspMI
bstEII hphI bspMI
3701 ATAGGGTCAC CATCACTGC AGGTCAAGTC AAAGCTTAGT ACATGGTATA GGTGCTACGT ATTTACTG GTATCAACAG AAACCGAGAA AAGTCCGAA
TATCCAGTG GTAGTGACG TCCAGTTGAG TTTCGAATCA TGTACCATAT CCAGCATGCA TAAATGTGAC CATAGTTGTC TTGGTCTT TTGAGGCTT
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K
scrFI
mvaI
ecoriI
dsav
bstNI aluI
apyI[dcM+]
maeIII
nlaIII
maeI
snaiI
bsaI
bsrI
maeI
rsal
dclI
aluI csp6I
hindIII
nlaIII
hphI
hphI bspMI
bstEII hphI bspMI
3701 ATAGGGTCAC CATCACTGC AGGTCAAGTC AAAGCTTAGT ACATGGTATA GGTGCTACGT ATTTACTG GTATCAACAG AAACCGAGAA AAGTCCGAA
TATCCAGTG GTAGTGACG TCCAGTTGAG TTTCGAATCA TGTACCATAT CCAGCATGCA TAAATGTGAC CATAGTTGTC TTGGTCTT TTGAGGCTT
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K
```

FIG. 48M



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
mspI
hpaII
bsaI
bsaWI
sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmII[dam-]
alwI[dam-]
nlaIV
bstYI/xhoII
bamHI
alwI[dam-] bsmFI
3801 ACTACTGATT TACAAAGTAT CCAATCGATT CTCTGGAGTC CCTTCTGGCT TCCTCTGGTC CGGTCTGGG ACGGATTTC CTCTGACCAT CAGCAGTCTG
TGATGACTAA ATGTTTCATA GGTTAGCTAA GAGACCTCAG GGAAGAGCGA AGAGACCTAG GCCAAGACCC TGCCTAAGT GAGACTGGTA GTCGTCAGAC
51 L L I Y K V S N R F S G V P S R F S G S G S G T D F T L T I S S L
tfII
hinFI
taqI
clal/bsp106 pleI
bspDI[dam-] hinFI
3901 CAGCCAGAAG ACTTCGCAAC TTATTACTGT TCACAGAGTA CTCATGTCCT GCTCAGCTT GCACAGGTA CCAAGGTGGA ACTGTGGCTG
GTGGGTCTTC TGAAGCGTTG AATAATGACA AGTGTCTCAT GAGTACAGG CGAGTGCAA CCTGTCCCAT GGTCCACCT CTAGTTTGT TGCACCCGAC
84 Q P E D F A T Y Y C S Q S T H V P L T F G Q G T K V E I K R T V A A
mboII
bpuAI
bbsI
mboII aciI
4001 CACCATCTGT CTTTCATCTC CCGCCATCTG ATGACAGATT GAAATCTGGA ACTGCTTCTG TTGTGTGCTT GGTGAATAAC TTCTATCCCA GAGAGGCCAA
GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGAAGAC AACACACGGA CCACTATTG AAGATAGGT CTCTCCGTT
118 P S V F I F P P S D E Q L K S G T A S V V C L L N N F Y P R E A K
rsal
csp6I
nlaIV
kpnI styI
hgiCI
banI bsaJI
asp718
acc65I
maeII
bsrBI
aciI
bsmFI
nlaII
scal
rsal
csp6I
scal
mboII
bpuAI
bbsI
mboII aciI
xmnI
asp700
cac8I
asp700
haeIII/palI
haeI
mnII
```

FIG. 48N

[illegible]

FIG. 480

FIG. 48P



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

sau3AI
mboI/hdeII(dam-)
dpnI(dam+)
sau96I
haeIII/palI
asul
dpnII(dam-)
pvuI/bspCI
mnII aciI
mboII cac8I mcrI
earI/ksp632I bsiEI
CGAAGAGGCC CGCACCAGTC GCCCTTCCCA ACAGTTGCCGT
CGGTGGCTAG CCGGAAGGGT TGTCAACGCCA
5001 TGGCGTTACC CAACCTTAATC GCCTTGACGC ACATCCCCCC TTCCGCCAGCT GCGGTAATAG
ACCGCAATGG GTTGAATTAG CCGAACGTCG TGTAGGGGGG AAGCGGTCGA CCGCATTATC
cac8I
aluI
pvuII
nspBII
cac8I
fokI
fnu4HI
bsoFI
bbvI
tru9I
msei
maeIII
5101 AGCCTGAATG GCGAATGGCG CCTGATGCGG TATTTTCTCC TTACGCATCT GTGCGGTATT TCACACCGCA TAGTCAAAG CAACCATAGT ACGCGCCCTG
TCGGACTTAC CGCTTACGCG GGACTACGCC ATAAAGAGG AATGGGTAGA CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TCGCGGGGAC
hinPI
hhaI/cfoI
nlaIV
nari
kasi
hinII/acyI
hgiCI
haeII
bani
sfaNI
bglI
5201 TAGCGGCGCA TTAAGCGCGG CGGGTGTGGT GGTACGCGC AGCGTGACCG CTACACTTGC CAGCGCCCTA GCGCGCGCTC CTTTCGCTTT CTTCCTCTTC
ATCGCGCGCT AATTCGCGCG GCCACACCA CCAATGGCGG TCGCACTGCG GATGTGAACG GTCGGGGGAT CCGCGGCGAG GAAAGCGAAA GAAGGAAGG
hinPI
thai
fnuDII/mvnI
bstUI
scfI
bsh1236I
rsal hhaI/cfoI
csp6I bsiI
hinPI
thai
fnuDII/mvnI
bstUI
scfI
bsh1236I
rsal hhaI/cfoI
csp6I bsiI
hinPI
hhaI/cfoI
rmaI
hinPI haeII
hhaI/cfoI bsrBI
haeII maeI aciI
cac8I bfaI cac8I
mboII

```

FIG. 48R

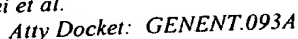


FIG. 48S



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

        sau3AI      nspBII      sau3AI      mboI/ndeII[dam-]      maeII      hgiAI/asphi
        mboI/ndeII[dam-]      dpnI[dam+]      psp1406I      bsp1286      tru9I
        bstYI/xhoII      dpnII[dam-]      xnnI      bsiHKAI      msei
        bsrI dpnII[dam-]      alwI[dam-]      asp700      bmyI      ahaIII/draI
        bssSI      maeIII      taqI      aciI      bstYI/xhoII      mboII      ahaIII/draI
        6201 CACGAGTGGG TTACATCGAA CTGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTCGCC CCGAAGAAGC TTTTCCATG ATGAGCACAT TTAAAGTTCT
        GTGCTCACCC AATGTAGCTT GACCTAGAGT TGTGCGCAAT TGTGCGCAAT CTAGGAACATC TCAAAAGCGG GGCCTTCTTG AAAAGGTTAC TACTCGTGAA AATTTCAGA

        scrFI
        aciI
        thal
        fnuDII/mvnI
        bstUI
        bsh1236I
        hinPI
        hhaI/cfoI
        6301 GCTATGTGGC GGGGTATTAT CCCGTGATGA CGCCGGGGCA GAGCAACTCG GTGCCCGCAT ACACATATTCT CAGAACTACT TGTTTGAGTA CTCACCAAGTC
        CGATACACCG CGCATATAATA GGGCACTACT GGGGCCCGTT CTCCTTGAGC CAGCGCGGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCTAG

        rsaI      csp6I      bsrI      scaI      hphI      maeIII
        6401 ACAGAAAGC ATCTTACGGA TGGCATGACA GTAAGAGAAAT TATGCAGTGC TGCCATAACC ATGAGTGATA ACACCTGGGC CAACTTACTT CTGACAAACGA
        TGTCTTTTCG TAGAATGCCT ACCGTAATGCT ACCGTAATGCT CATTCTCTTA ATACTCAGC ACGGTATTGG TACTCACTAT TGTGACGCCG GTTGAATGAA GACTGTGCT

        fnu4HI      bsoFI      bsvI      mslI      nlaIII      aciI      bsiEI
        sau3AI      mboI/ndeII[dam-]      dpnI[dam+]      dpnII[dam-]      pvuI/bspCI      mcrI      bsiEI
        6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTT TGCACAACTT GGGGATCAT GTAACCTGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCAA
        AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTGTGA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT

        sau96I      avaII      asuI      mnlI      aluI      aciI      nlaIII      sau3AI      maeIII      mspI
        mboI/ndeII[dam-]      dpnI[dam+]      dpnII[dam-]      dpnII[dam-]      dpnII[dam-]      bsaWI
        6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTT TGCACAACTT GGGGATCAT GTAACCTGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCAA
        AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTGTGA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT
```

FIG. 48U

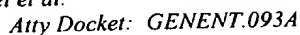


FIG. 48W

Restriction Enzyme	Sequence
7501	<p> 7501 TGAGCATTGA GAAAGCGCCA CGCTTCCCGA AGGGAGAAAG GCGGACAGGT ATCCGGTAAG CGGCAGGGTC GGAACAGGAG AGCGACAGAG GGAGTTCCA ACTCGTAACT CTTTCGGGT GCGAAGGGCT TCCCTCTTTC CGCCTGTCCA TAGGCCATTC GCGGTCCCAG CCTTGTCTCTC TCGGGTGCTC CCTCGAAGGT </p>
7601	<p> 7601 GGGGGAACG CCTGGTAATCT TTATAGTCCT GTCGGGTTTC GCCACCTCTG ACTTGAGCGT CGATTTTGTGATGCTCGTC AGGGGGGGG AGCCTATGGA CCCCCTTTGC GGACCATAGA AATATCAGGA CAGCCCAAG CGGTGGAGAC TGAACCTCGCA GCTAAAAACA CTACGAGCAG TCCCCCGGC TCGGATACCT </p>
7701	<p> 7701 AAAAGCCAG CAACGGCC TTTTACGGT TCCTGGCCTT TTGCTGGCCT TTGCTCACA TGTTCCTTCC TGCCTTATCC CCTGATTCG TGCGATAACCG TTTTGGGTC GTTGGCGG AAAAATGCCA AGGACCGAA AACGACCGA AACGAGTGT ACAAGAAAGG ACGCAATAGG GACTAAGAC ACCTATTGGC </p>
7801	<p> 7801 TATTACGCC TTTAGTGAG CTGATACCG TCGCCGACG CGAACGACCG AGCGAGCGA GTCAGTGAGC GAGGAAGCGG AAGAGCGCC AATACGCAA AATATGGCGG AAACCTCACT GACTATGGCG AGCGGGCTG GCTTGCTGGC TCGGCTCGCT CAGTCACTG CTCTTCGCTC TCTCGCGG TTATCGCTTT </p>



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```

thai
fnuDII/mvni
bstUI
bsh1236I
hinPI
hhaI/cfoI
thai
fnuDII/mvni          cac8I
bstUI haeIII/palI    aluI
bsh1236I             tru9I pvuII
mnlI   eaeI   tfII aseI/asnI/vspi
aciI   cfrI   hinI mseI   nspBII
7901  CCGGCTCTCC CCGGCGCTTG GCGGATTTCAT TAATCCAGCT GGCACGACAG GTTTCGCCGAC TGGAAAGCGG GCACTGAGCG CAACGCCAATT AATGTGAGTT
GGCGGAGAGG GCGCGGCAAC CCGCTAAGTA ATTAGGTGA CCGTGCTGTC CAAGGGCTG ACCTTTCGCC CGTCACTCGC GTTGGCGTTAA TTACACTCAA

scrFI
mvaI
ecorII
dsav
nlaIV bstNI
hgici apyI(dcm+)
bani bsaJI
mnlI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA
TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAATACGA AGGCCGAGCA TACACACAC CTTAACACTC GCCTATTGTT AAAGTGTCCT CTTTGTCTGAT

acuI
bsrBI
aluI
```

FIG. 48Y



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
tru9I
mseI
aseI/asnI/vspI
xmniI
nlaiII asp700
8101 TGACCATGAT TACGAATTAA (SEQ ID NO.68)
ACTGGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC): 1690 5947
acc65I(GGTACC): 2969 3967 4529
accI(GTMRAC): 823 1039 2738 4237
acII(CCGC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070

see hinI
acyI
afIIII/bfRI(CTTAAG): 786
afIIII(ACRYGT): 932 7758
ageI(ACCGGT): 1833
ahaII/bsaHI(GRCGYC): 988 1690 1858 5117 5947 6329
ahaII/draI(TTTAAA): 696 4935 6290 6982 7001
ahdI/eamII05I(GACNNNNNGTC): 2087 6865
alulI(AGCT): 5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
alw44I/snoI(GTGCAC): 1876 5651 6198 7444
```

FIG. 48Z



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

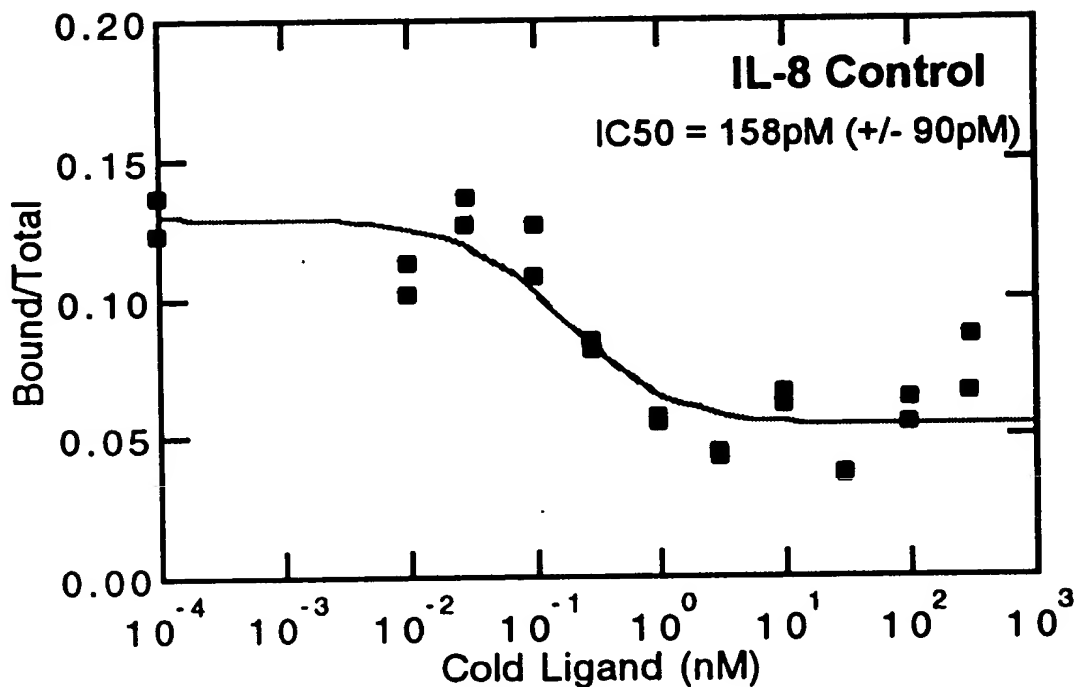


FIG. 49A

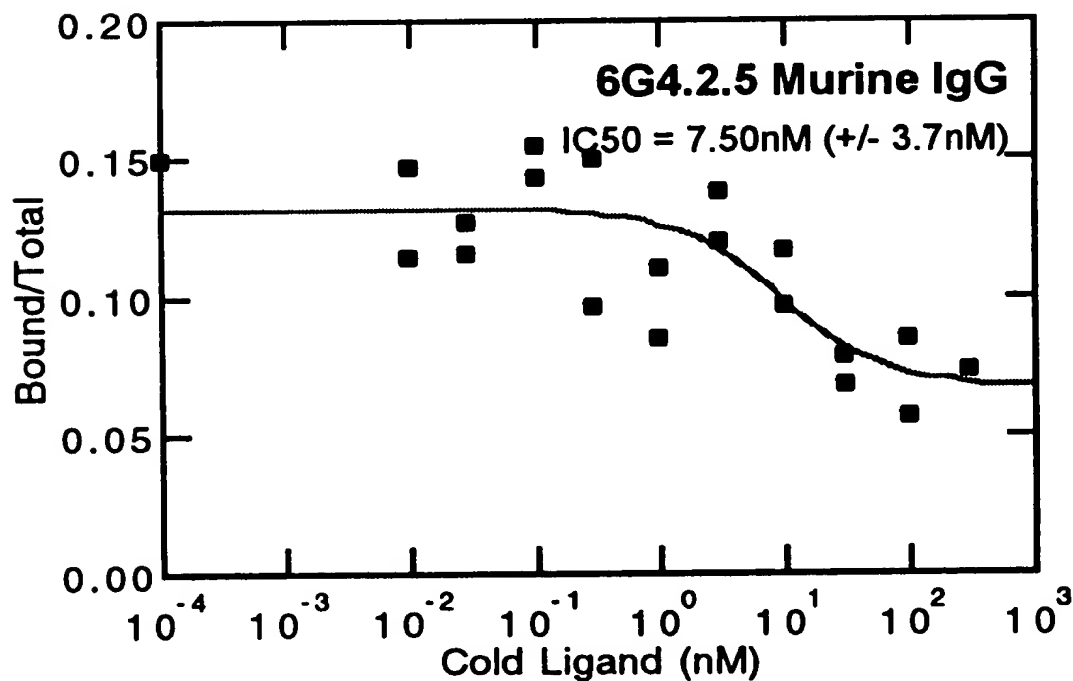


FIG. 49B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

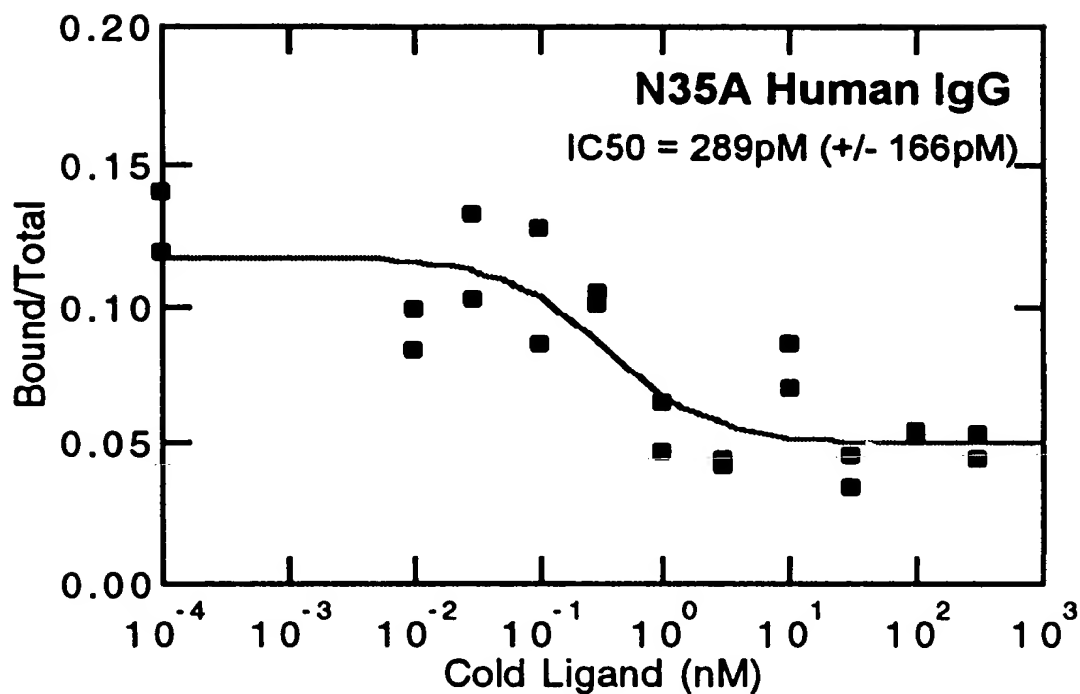


FIG. 49C

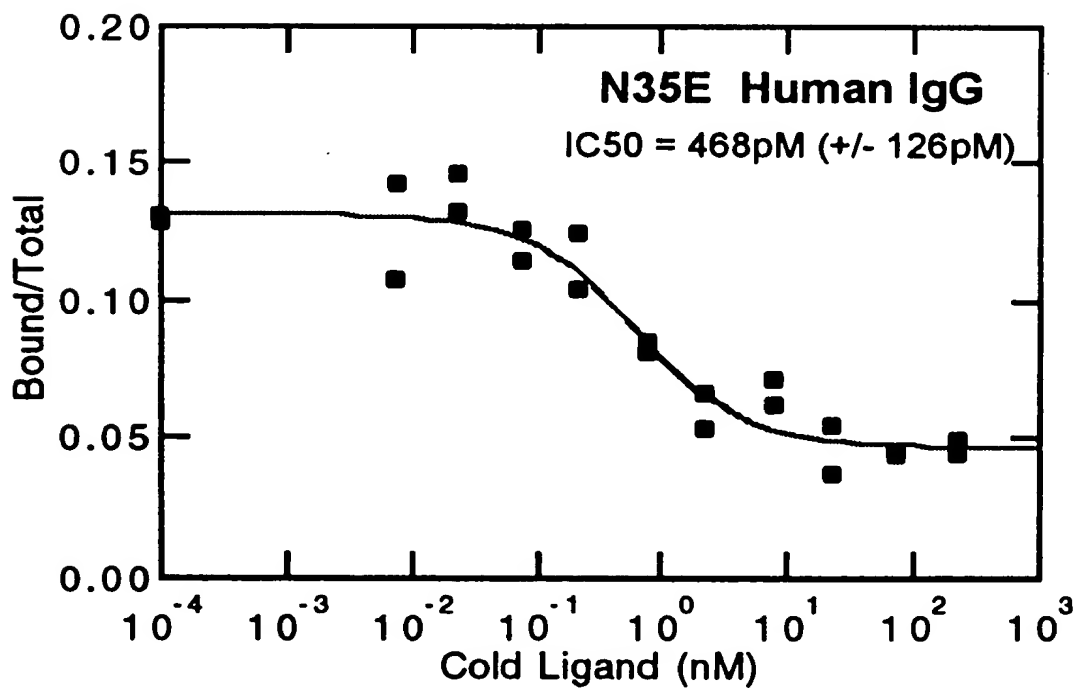


FIG. 49D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

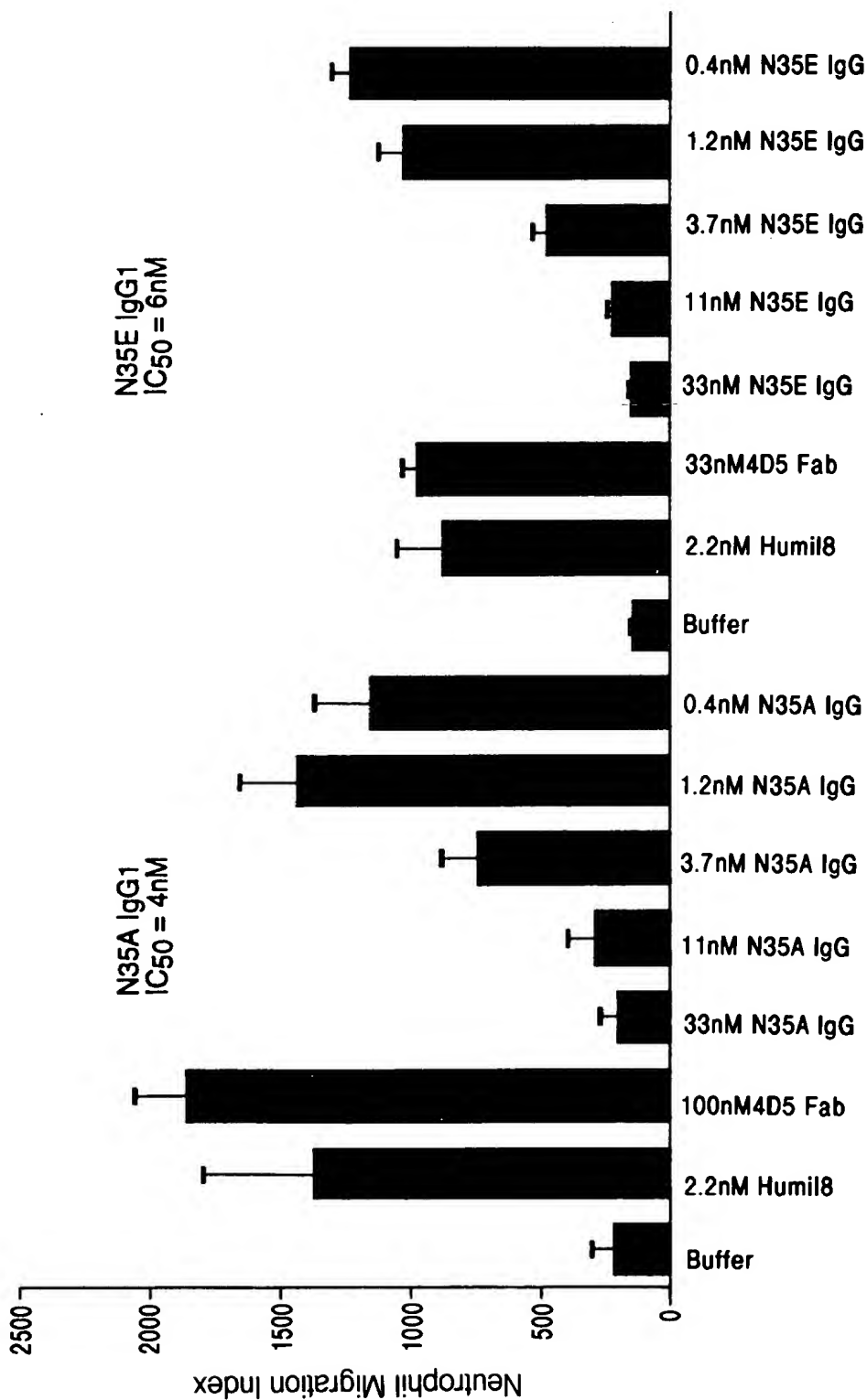


FIG. 50A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

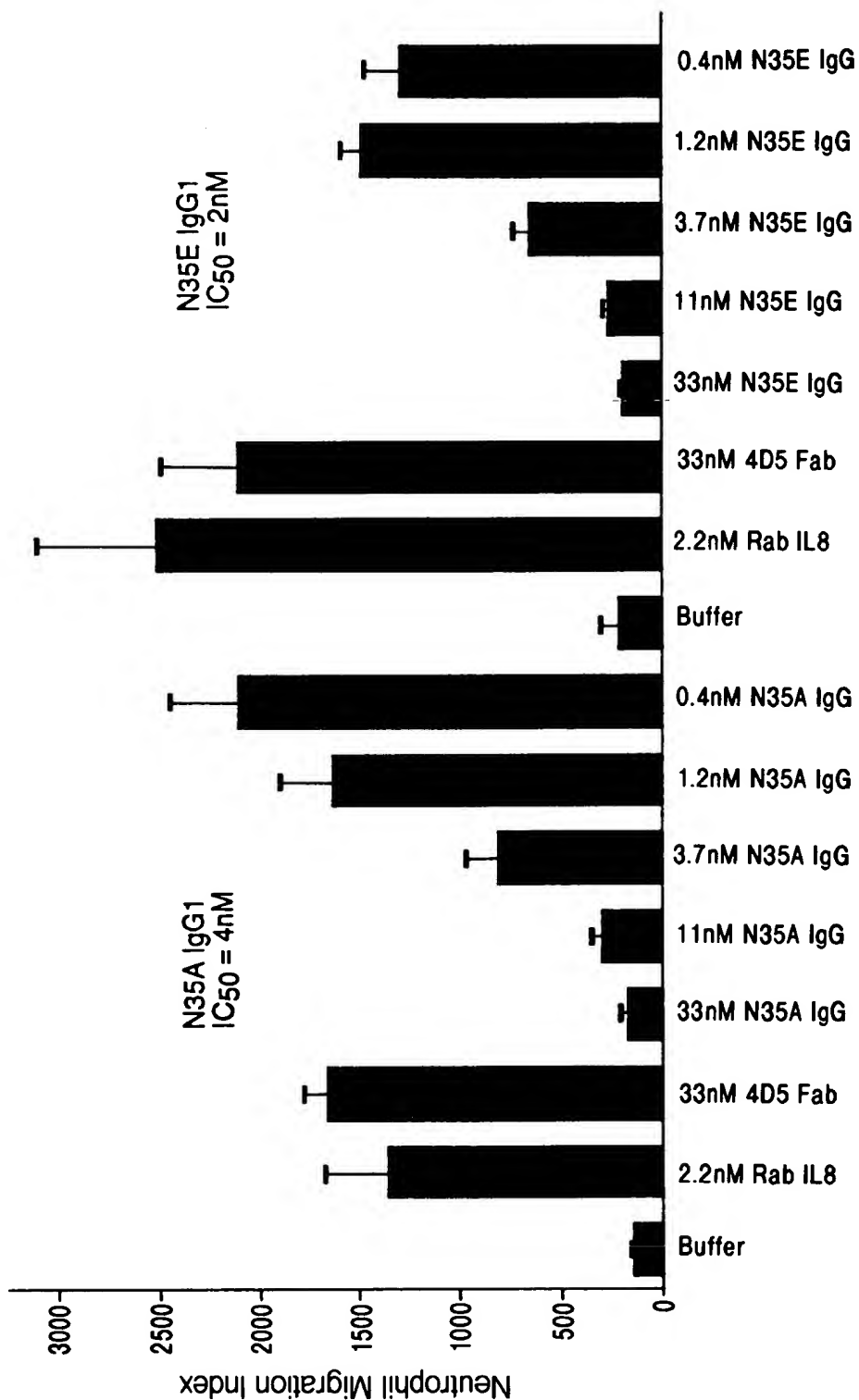


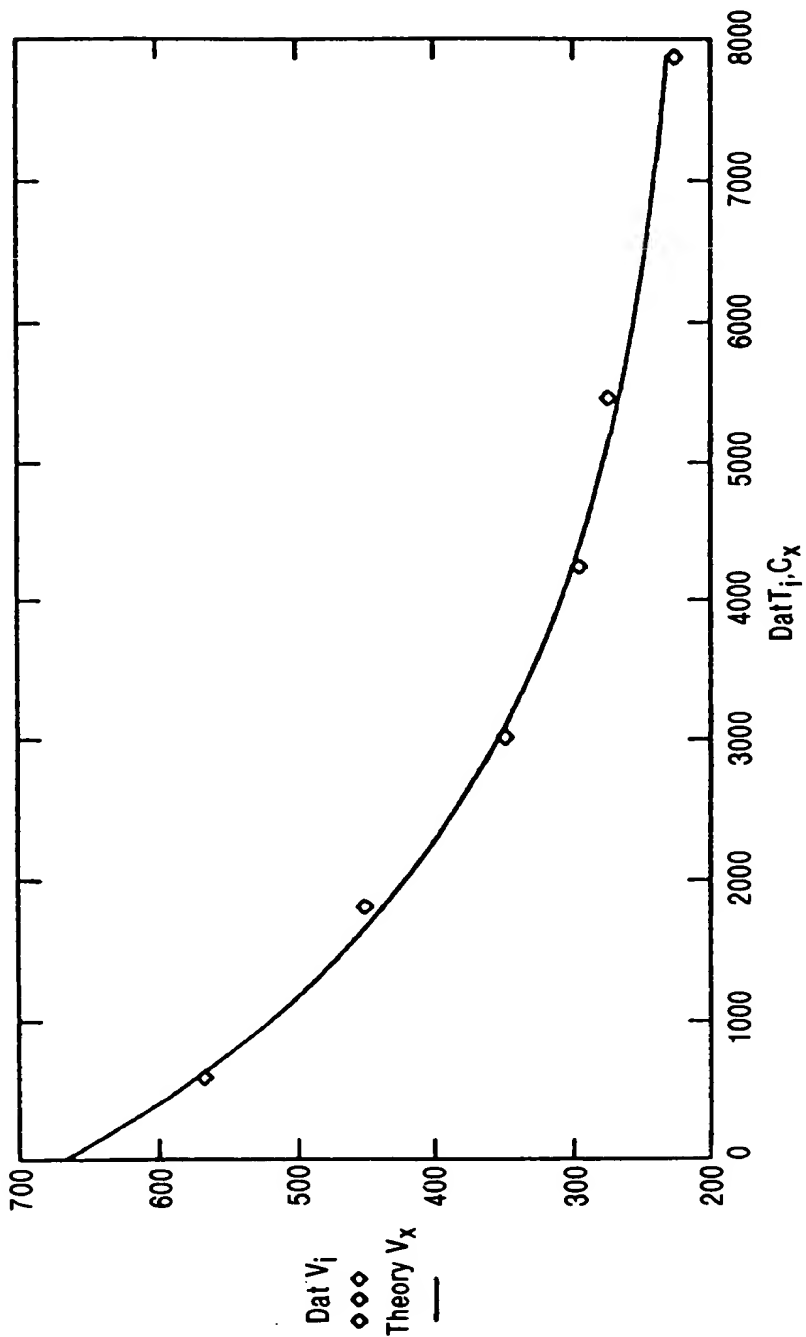
FIG. 50B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3x10 ⁵	2.9x10 ⁻⁴	350pM
6G4V11N35A-IgG1	8.7x10 ⁵	7.7x10 ⁻⁵	88pM
6G4V11N35E-IgG1	3.0x10 ⁶	1.4x10 ⁻⁴	49pM

FIG. 51



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

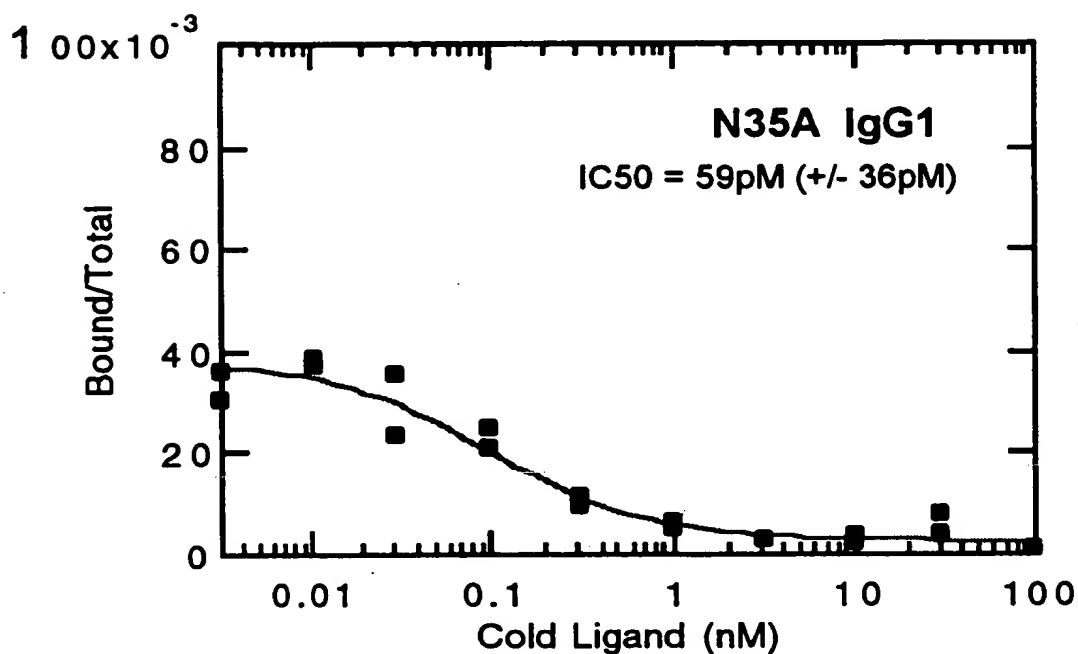


FIG. 52A

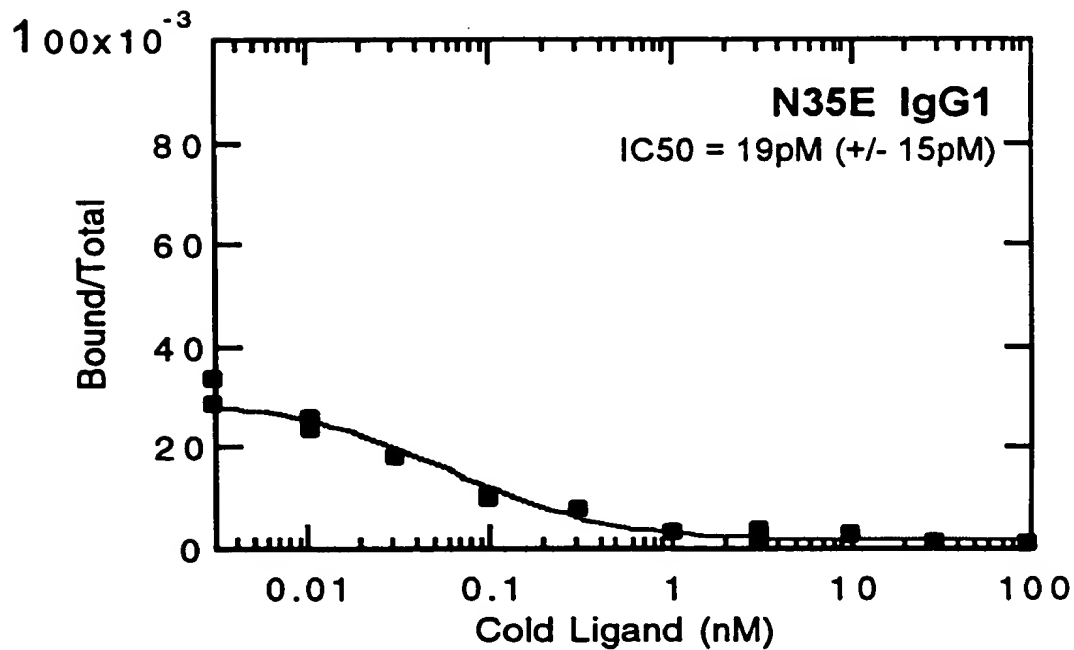


FIG. 52B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTCG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GCGGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCTGATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTTCG CACACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTGCTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTCG GGTGCTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTGA (SEQ ID NO.69)
TGAGTGTGTA CGGGCGGCACT
228 T H T C P P O (SEQ ID NO.70)

FIG. 53

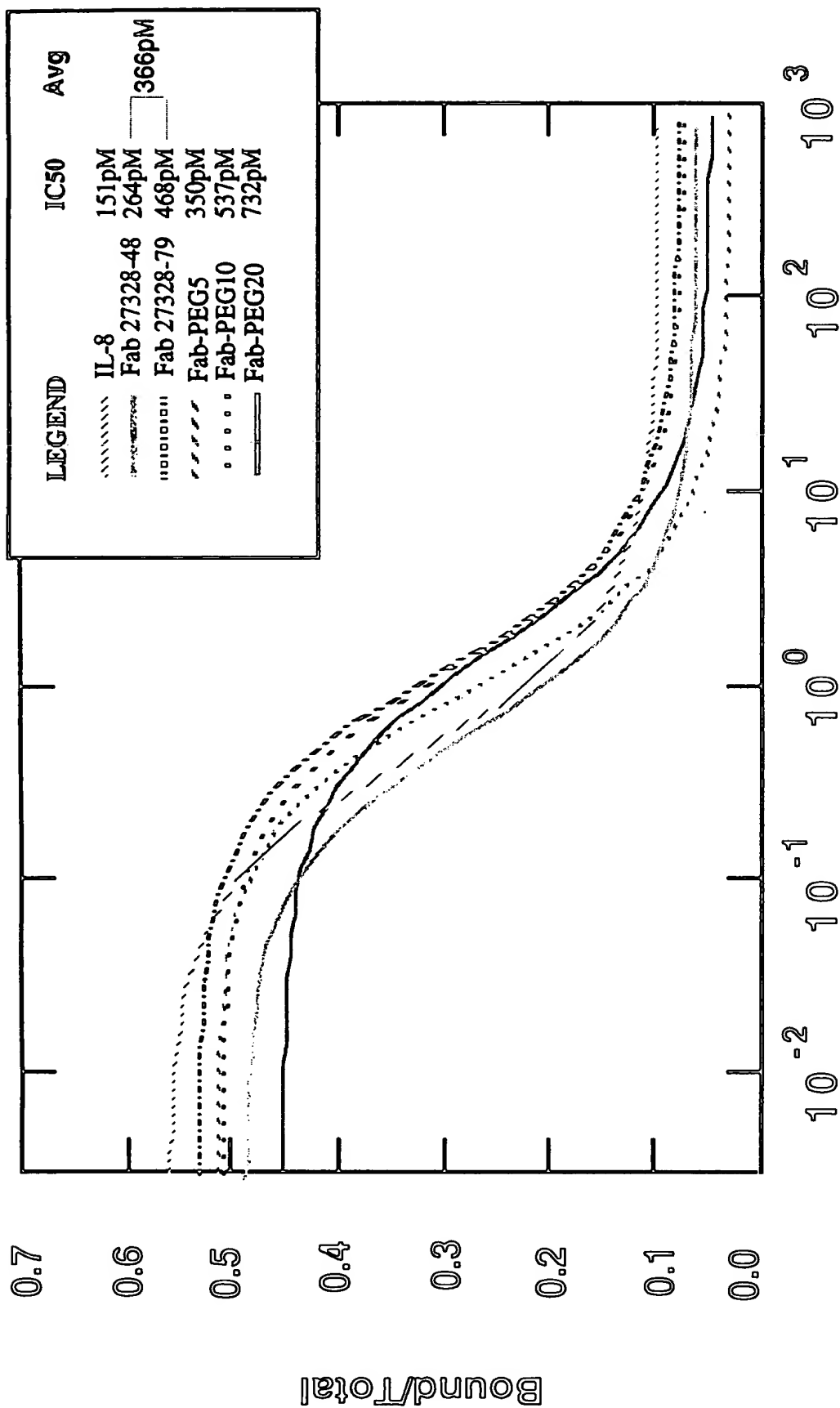


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

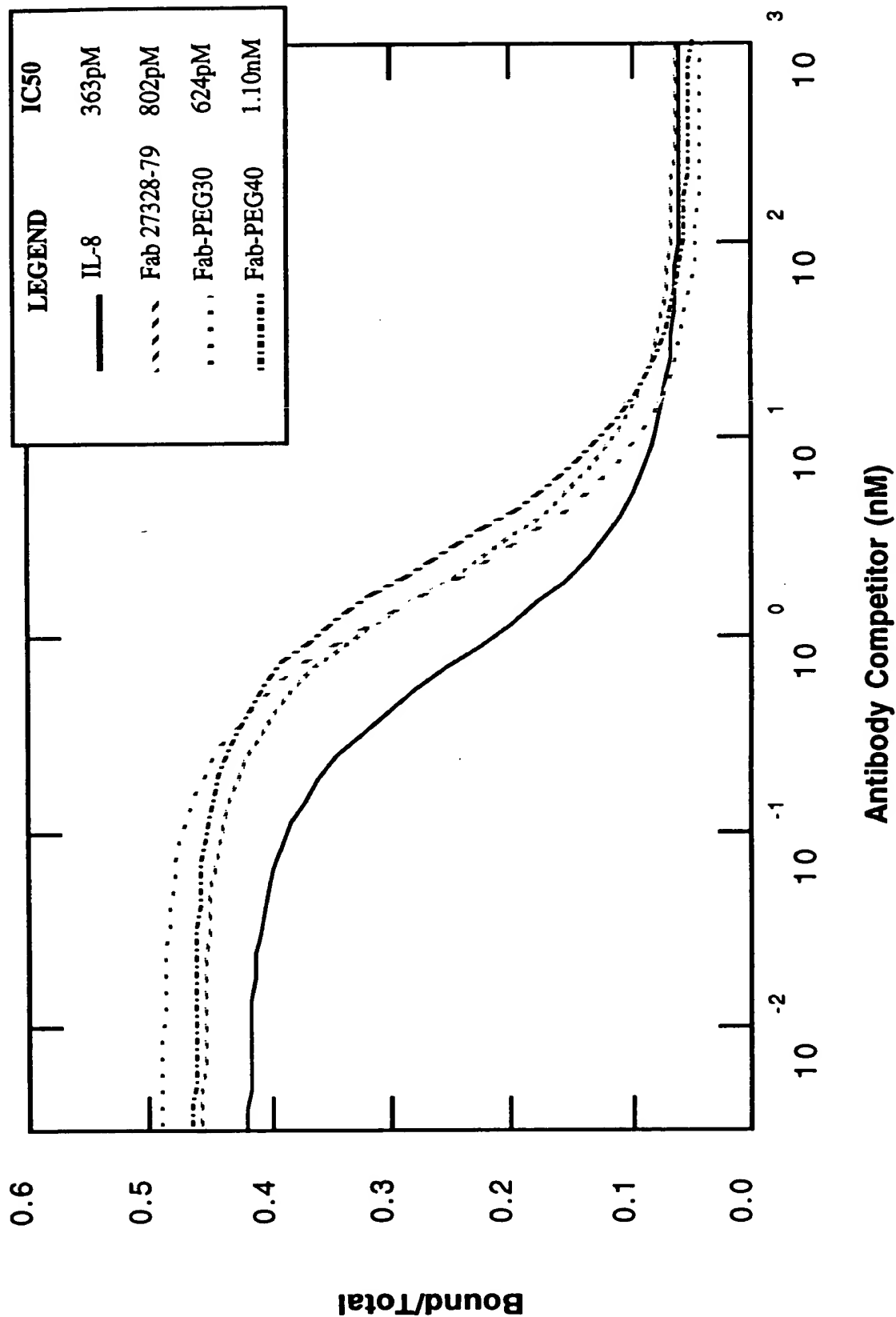


FIG. 54B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

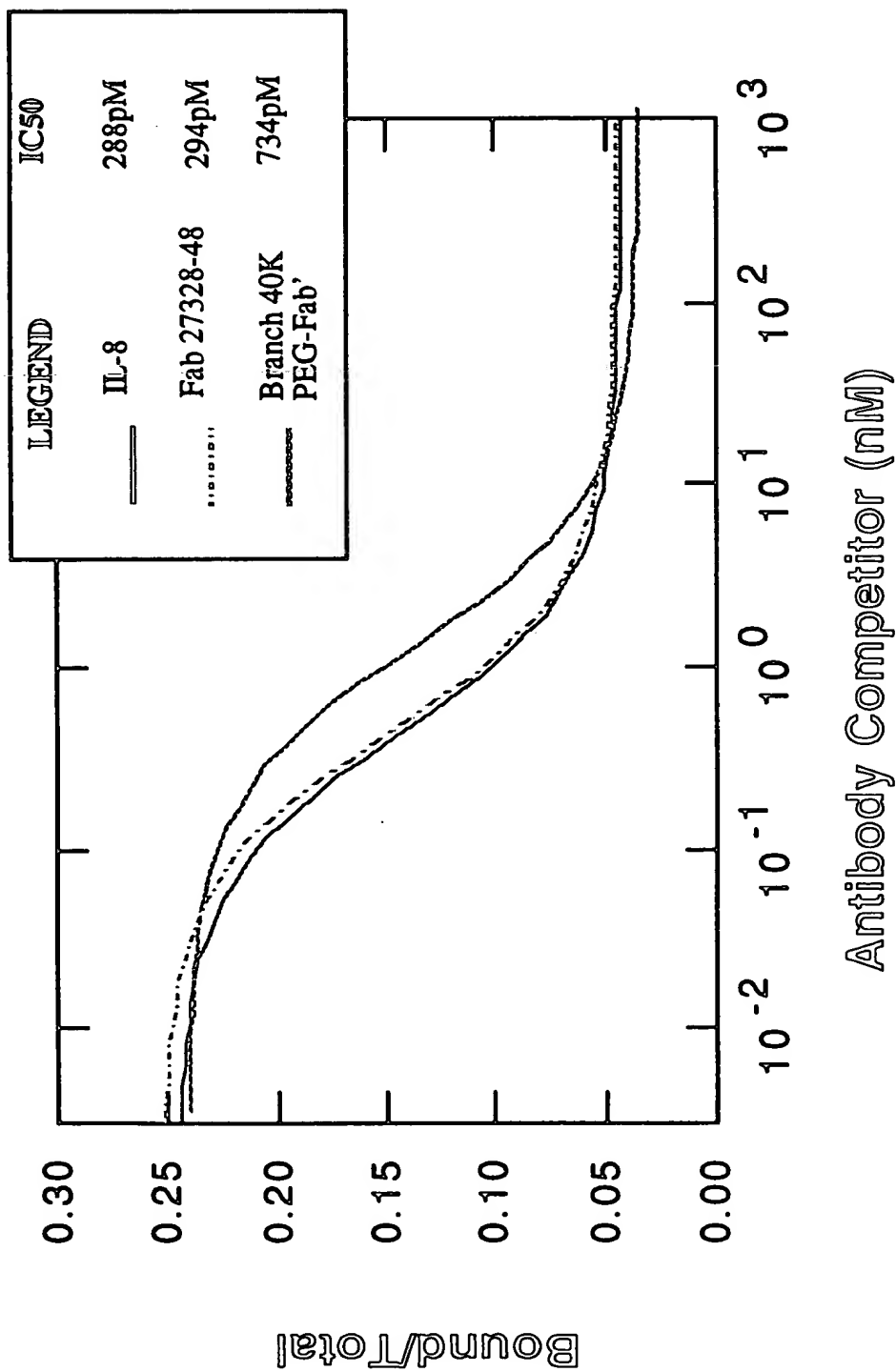


FIG. 54C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

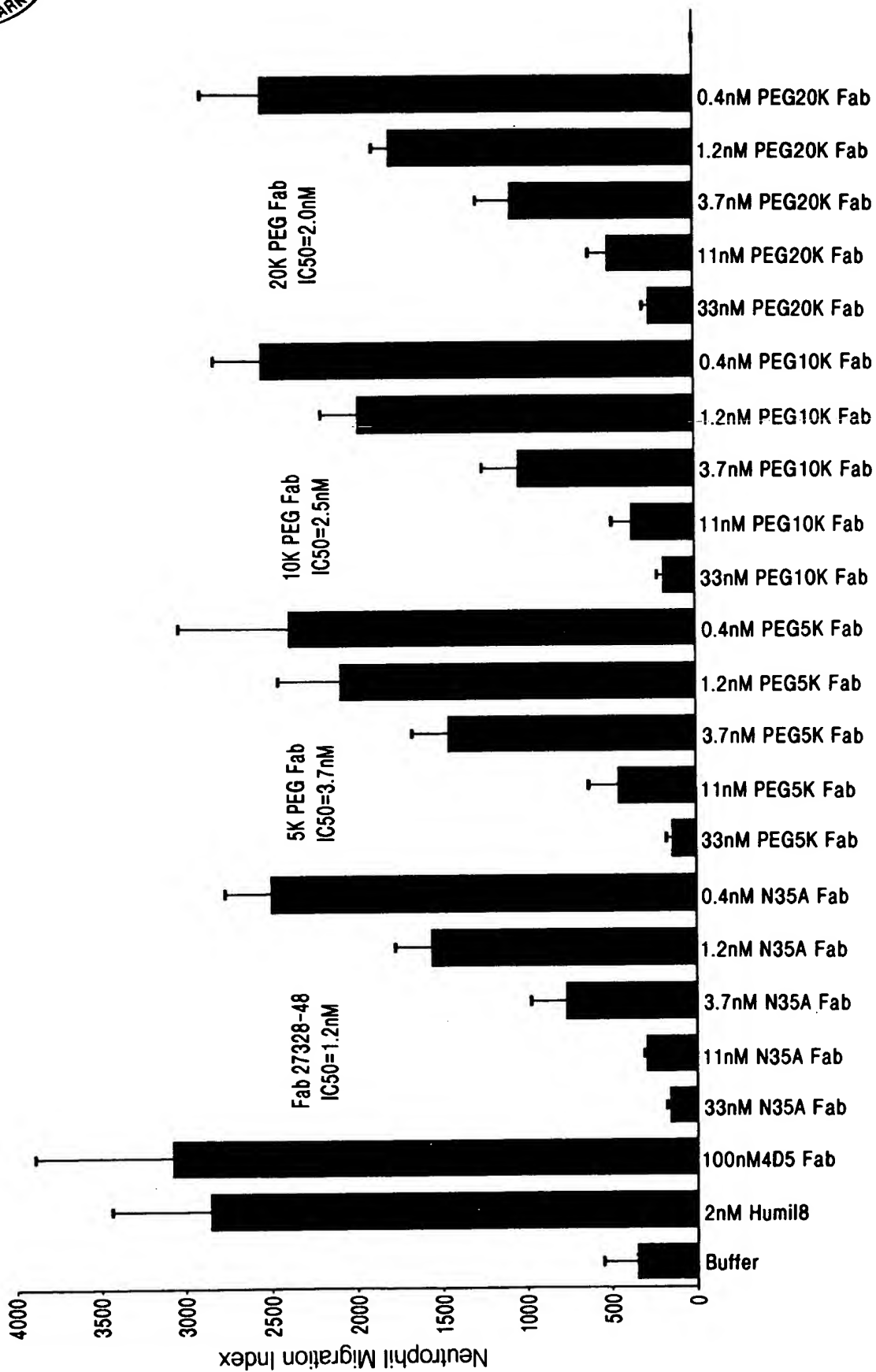


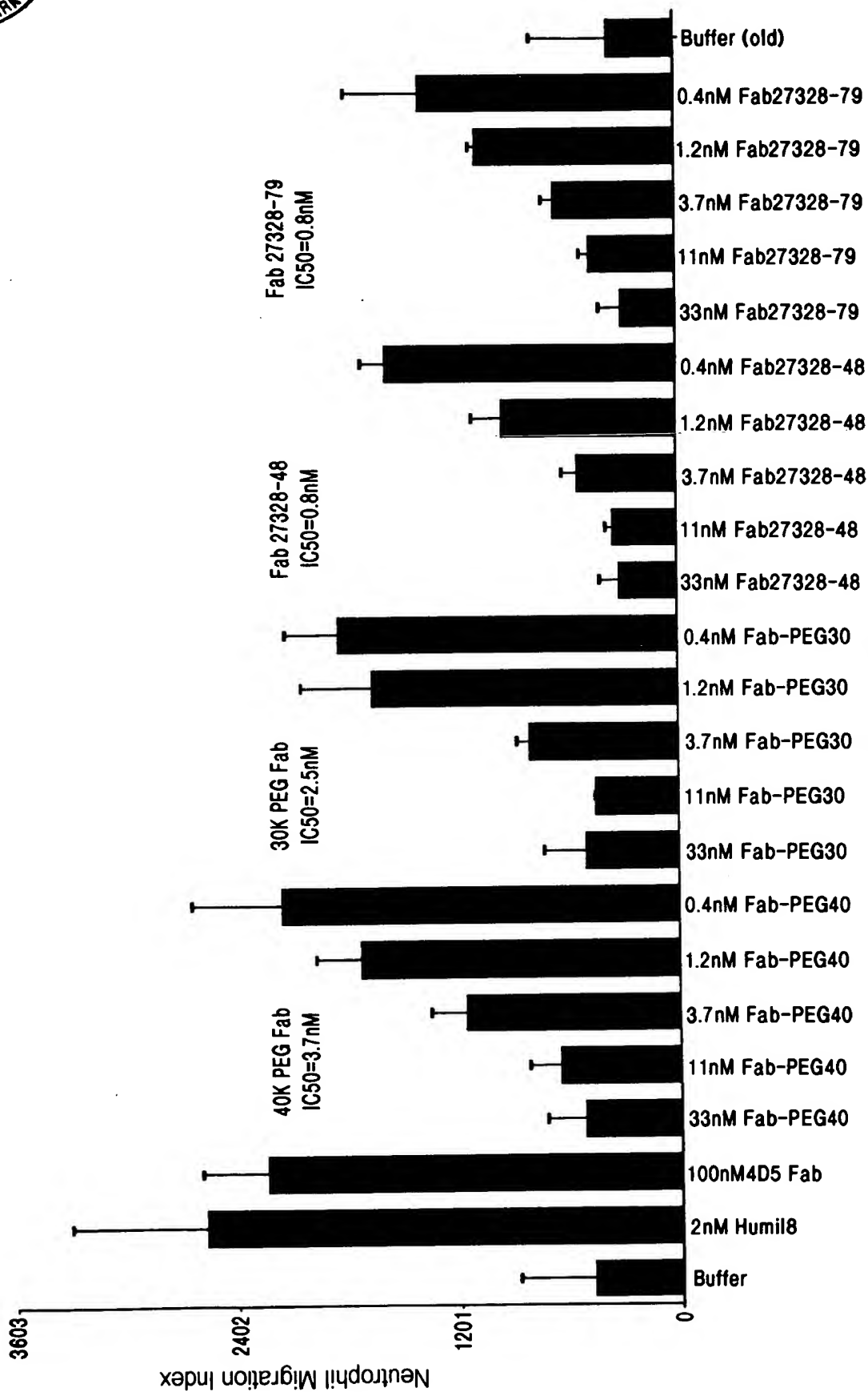
FIG. 55A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

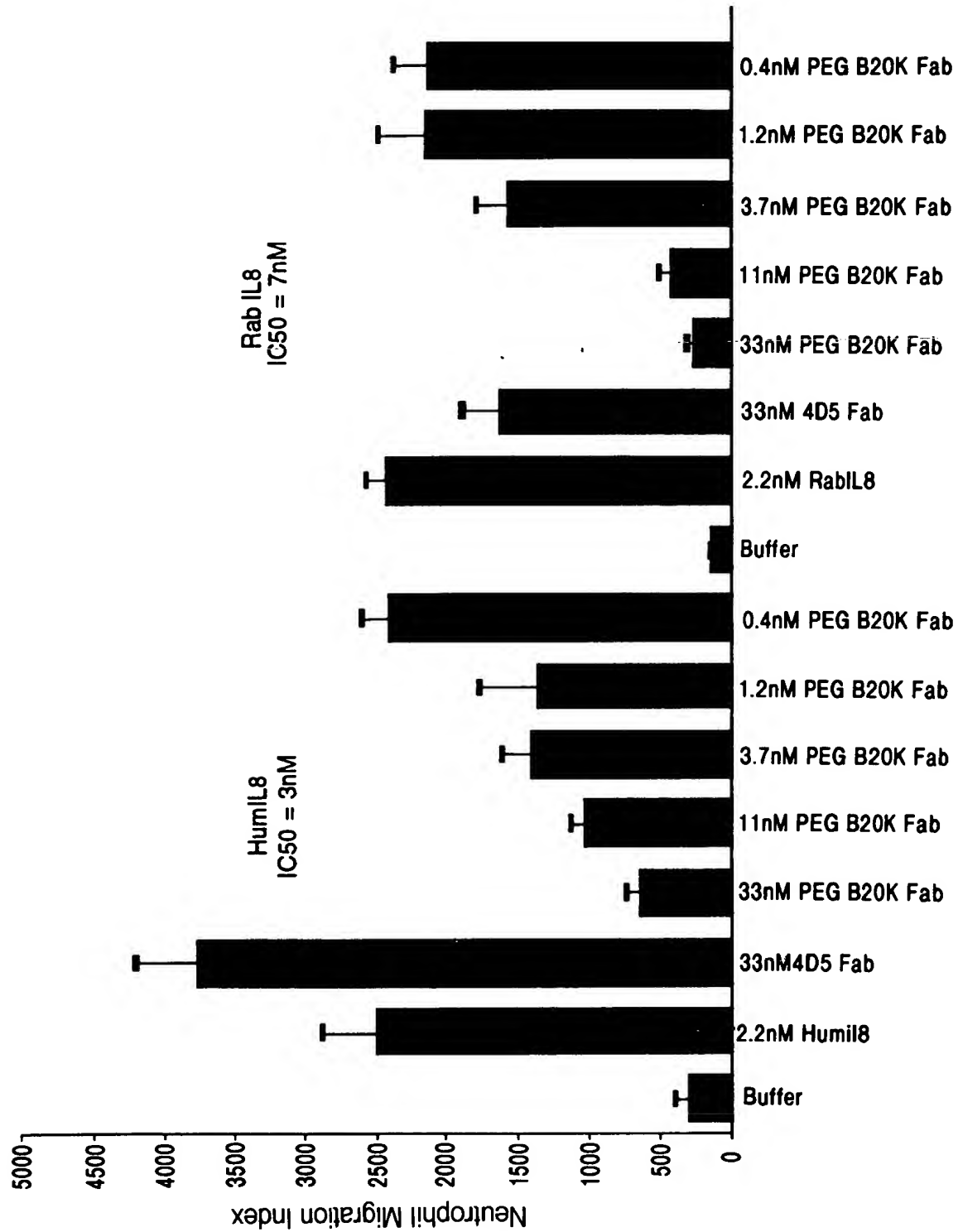


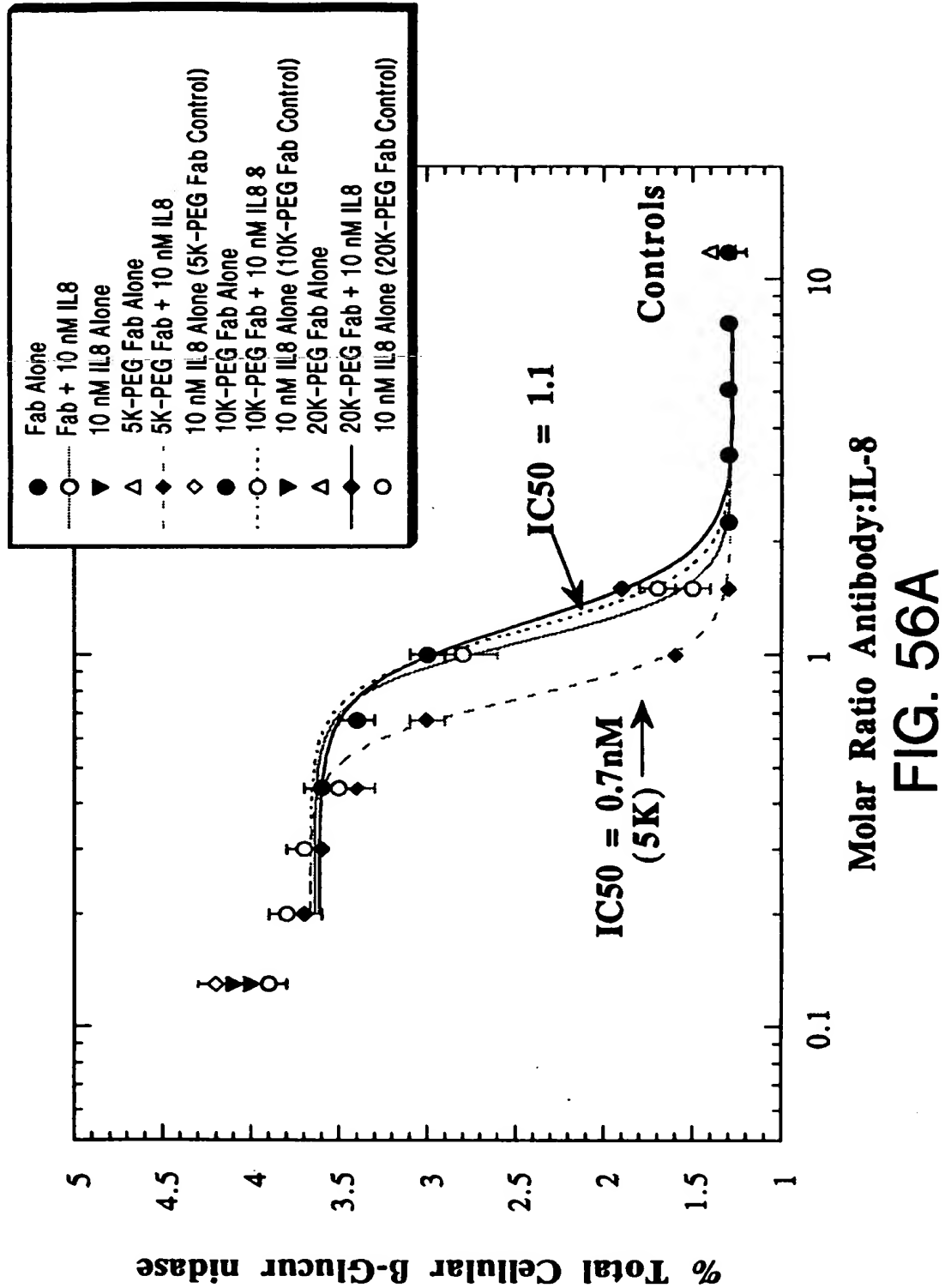
FIG. 55C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

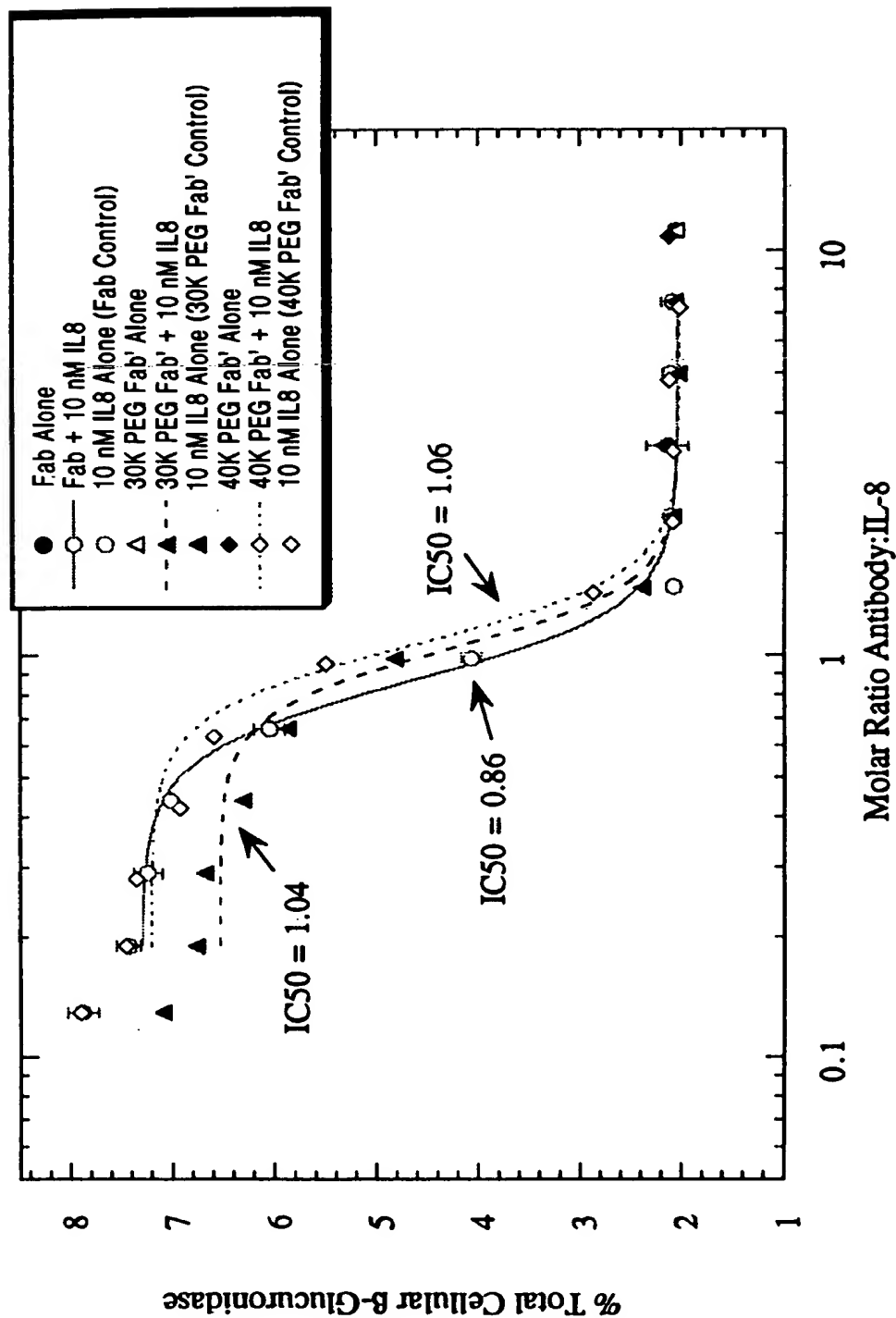


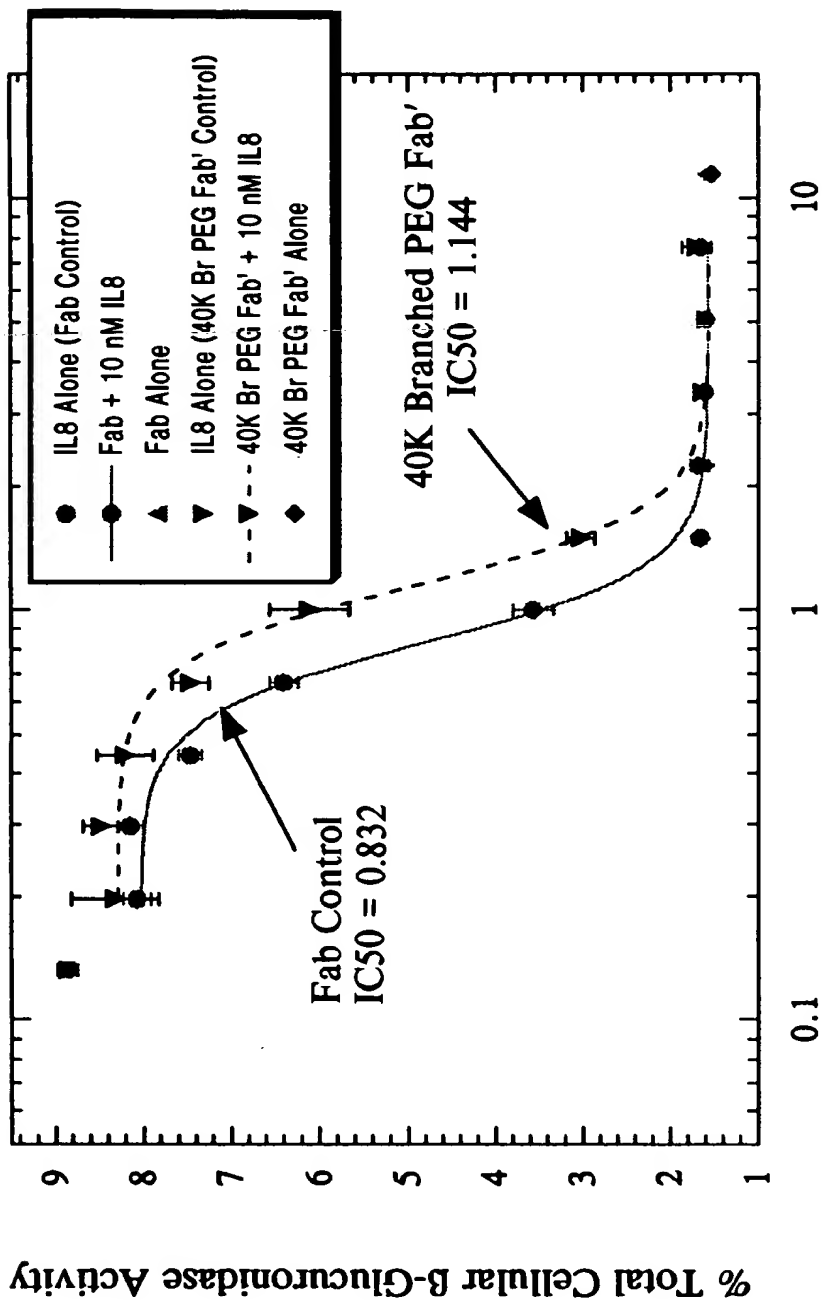
FIG. 56B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



Molar Ratio Antibody:IL8

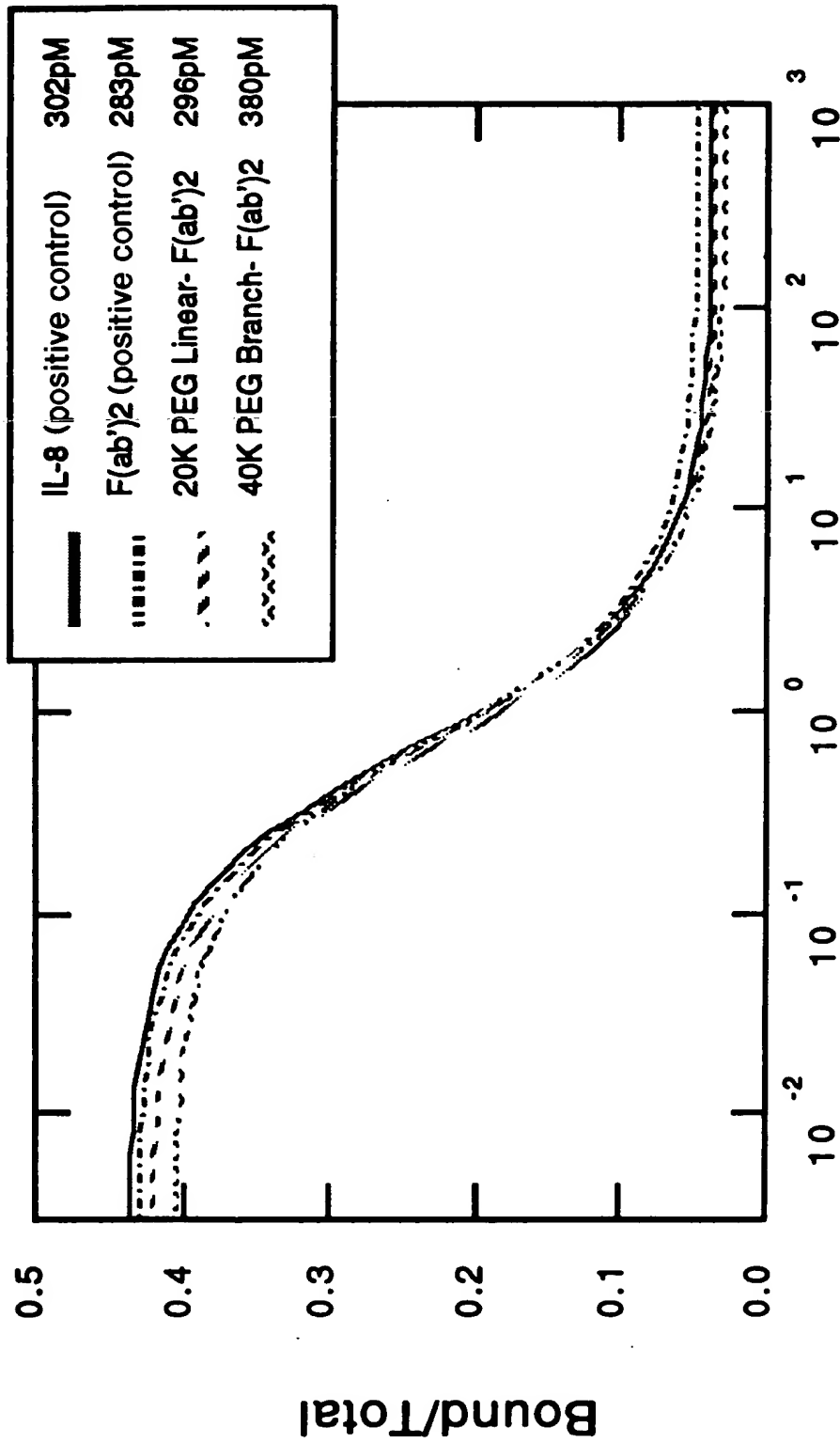
FIG. 56C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



Pegylated F(ab')₂ (nM)

FIG. 57A

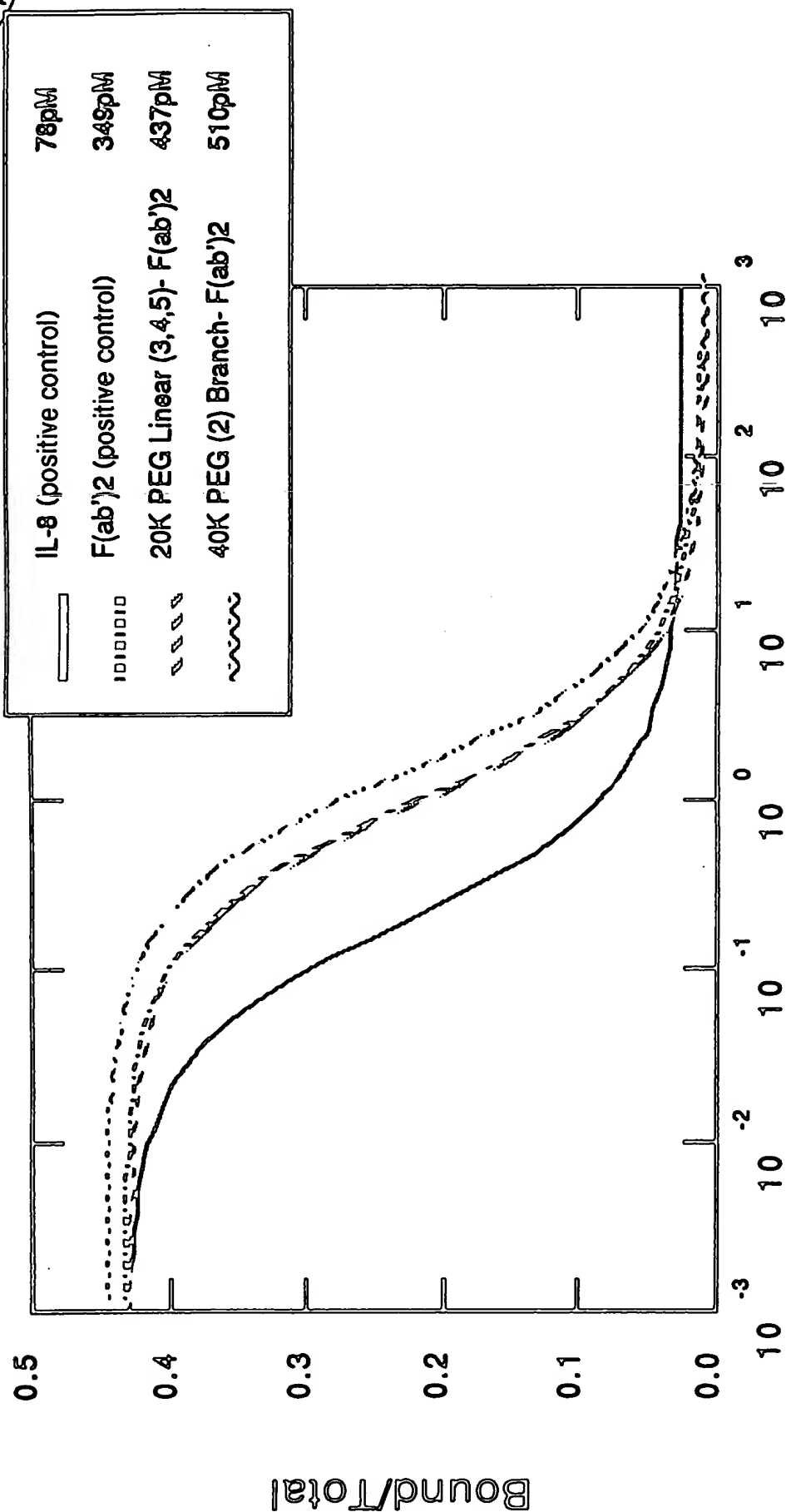


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



Pegylated F(ab')₂ (nM)

FIG. 57B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

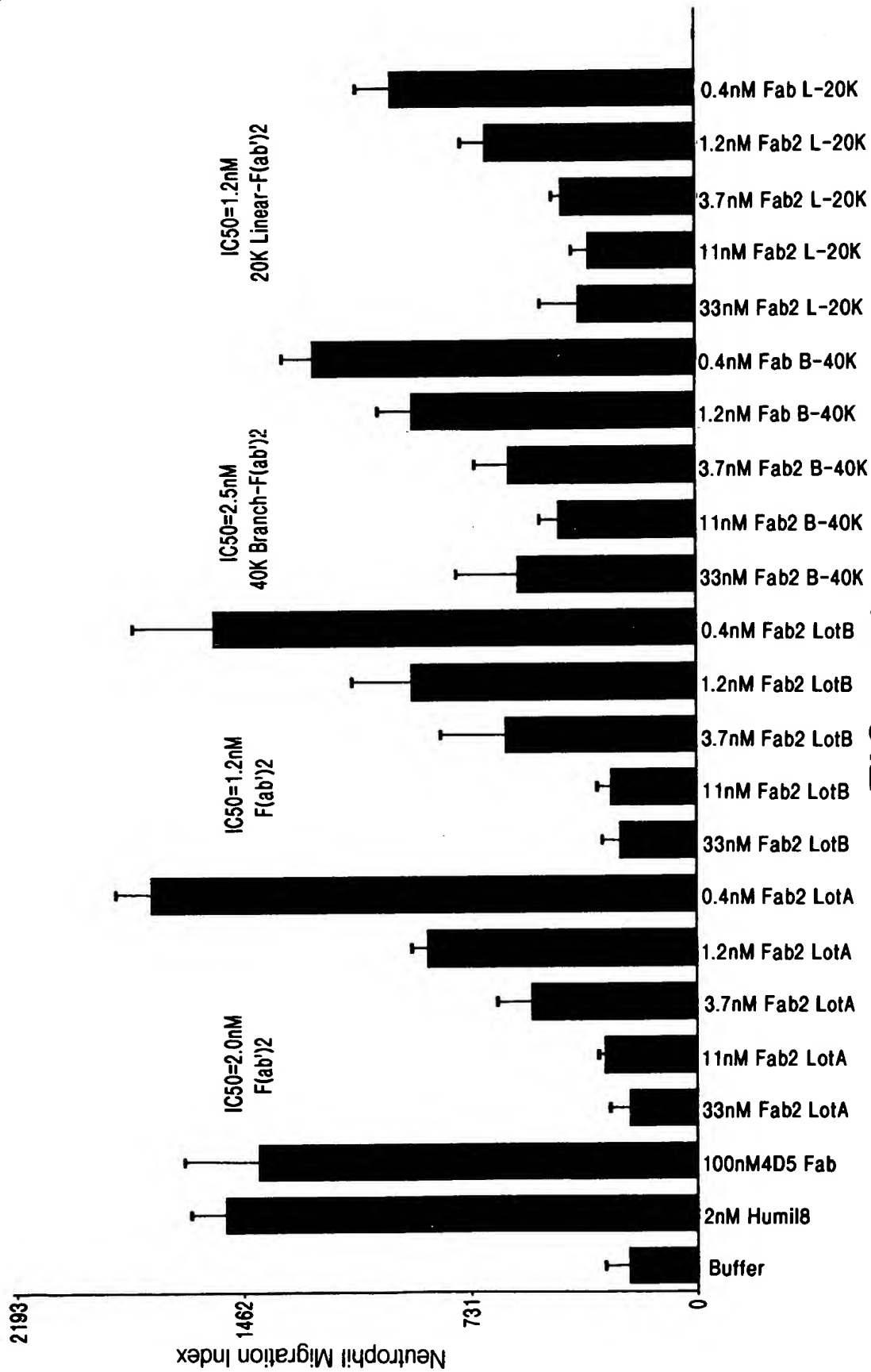


FIG. 58A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

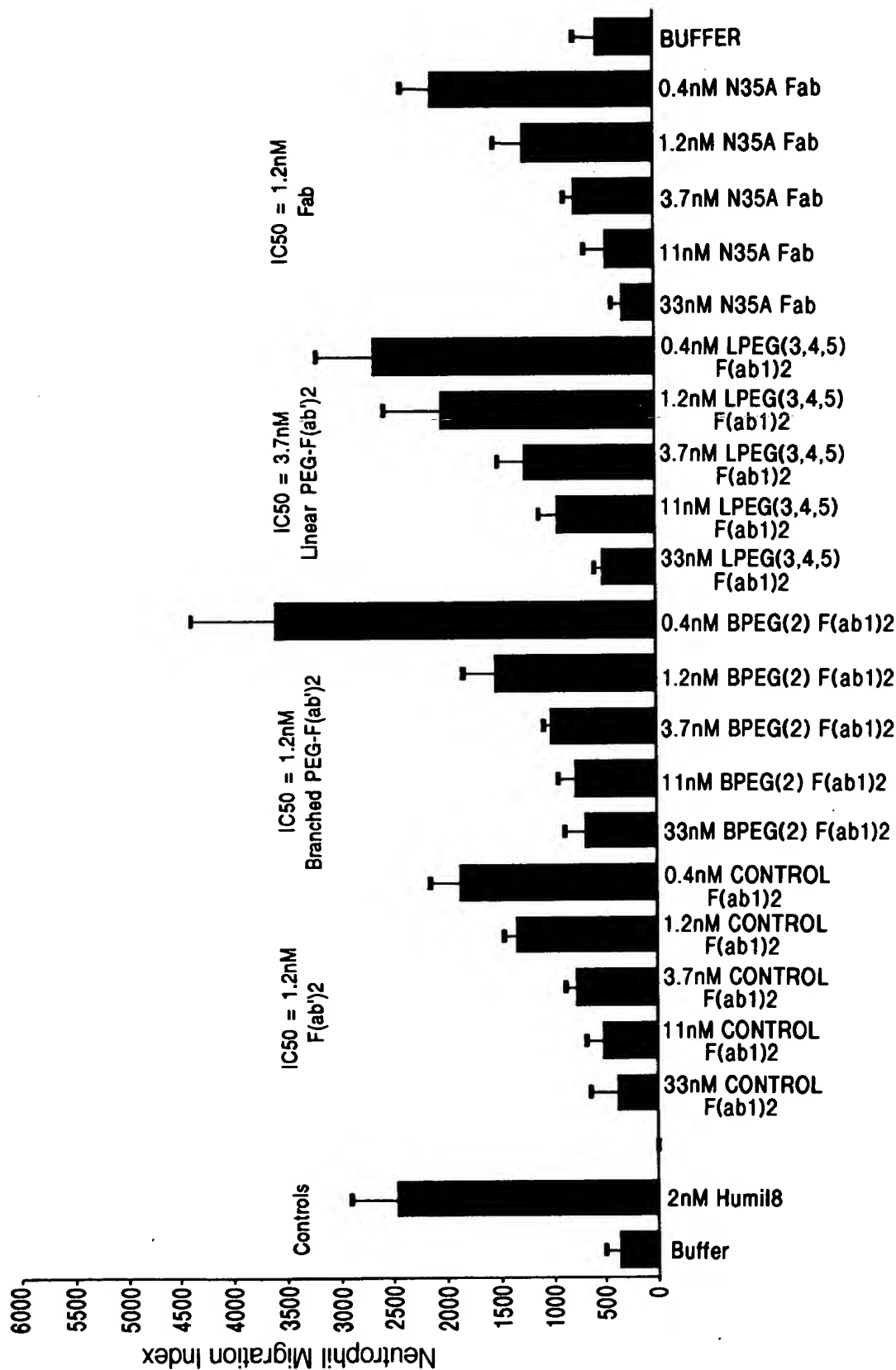


FIG. 58B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

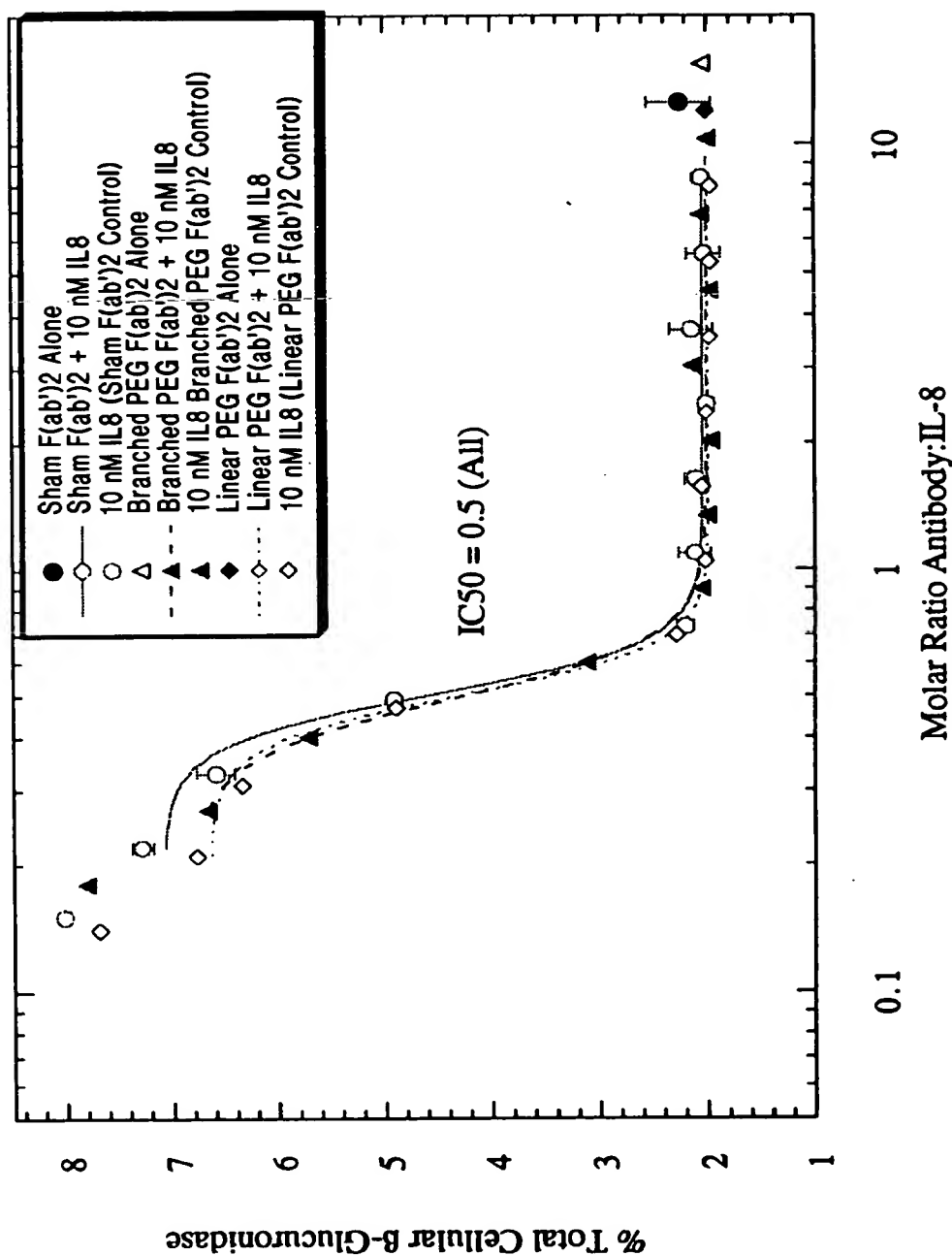


FIG. 59A

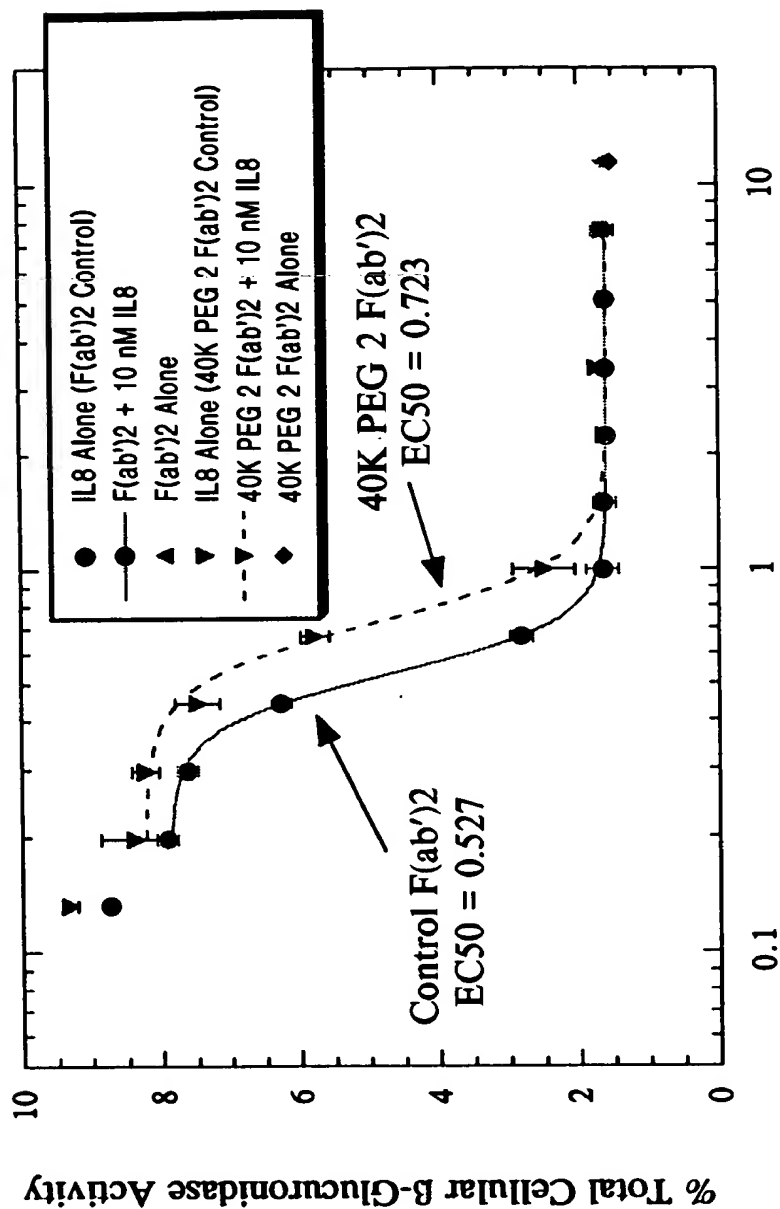


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



Molar Ratio Antibody:IL8

FIG. 59B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

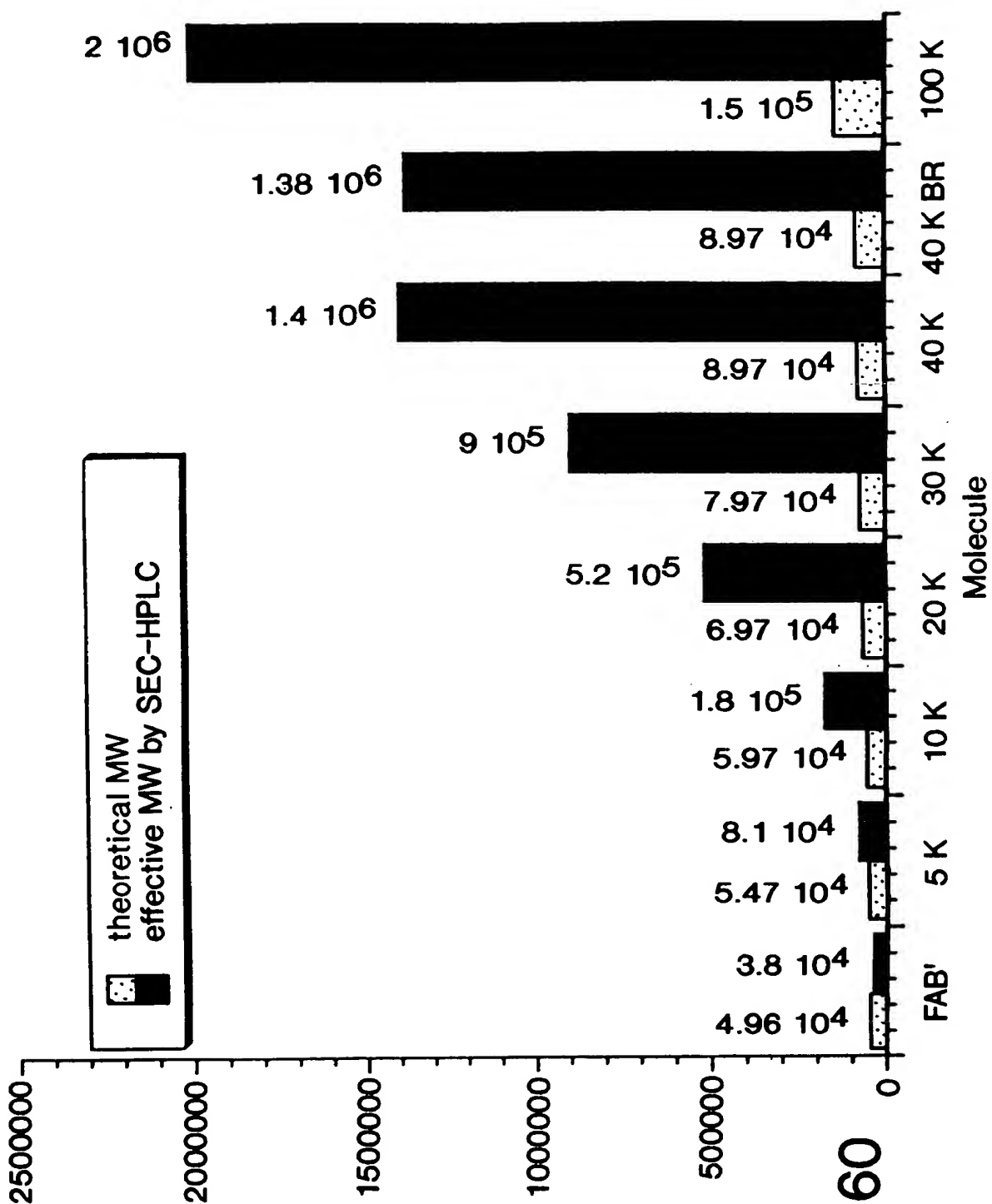
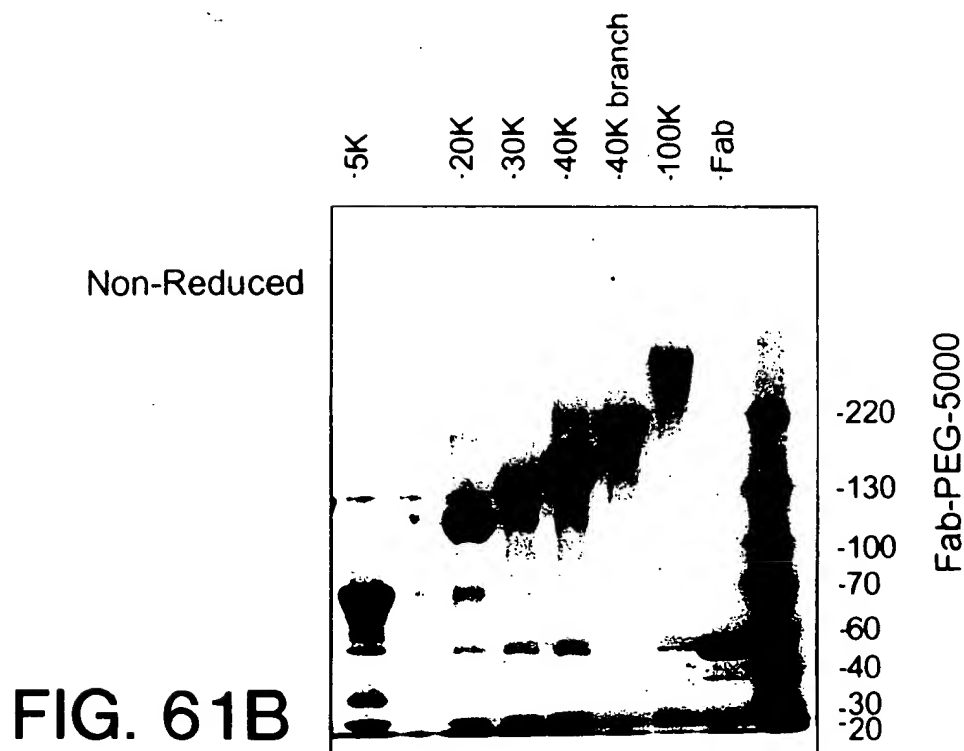
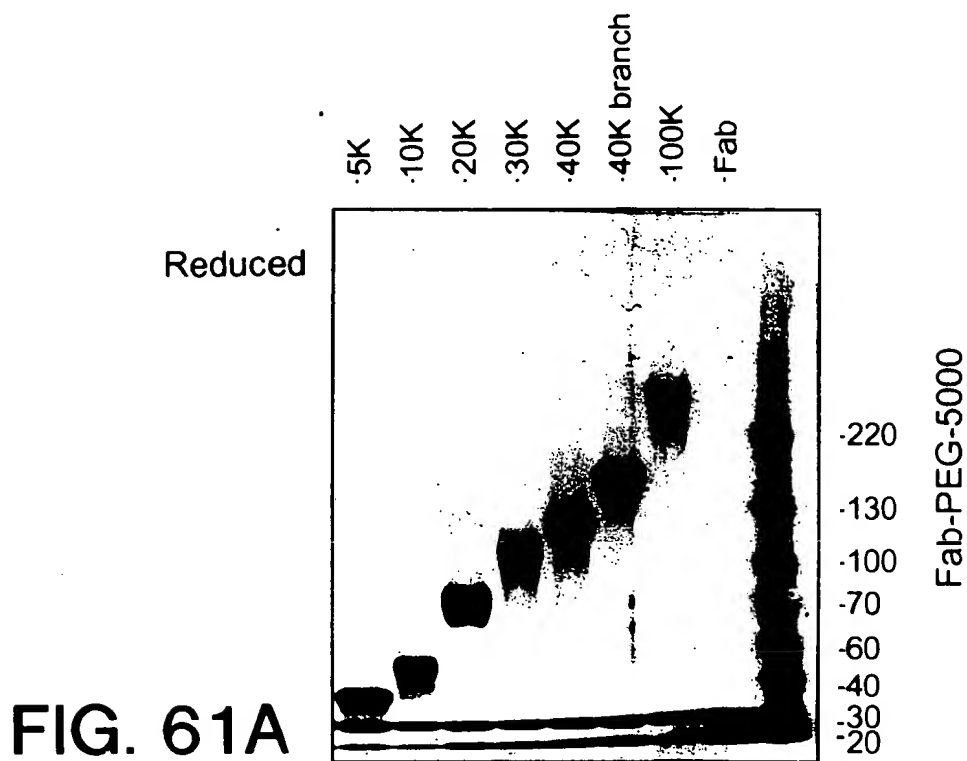


FIG. 60

MW (D)



10/21/02





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

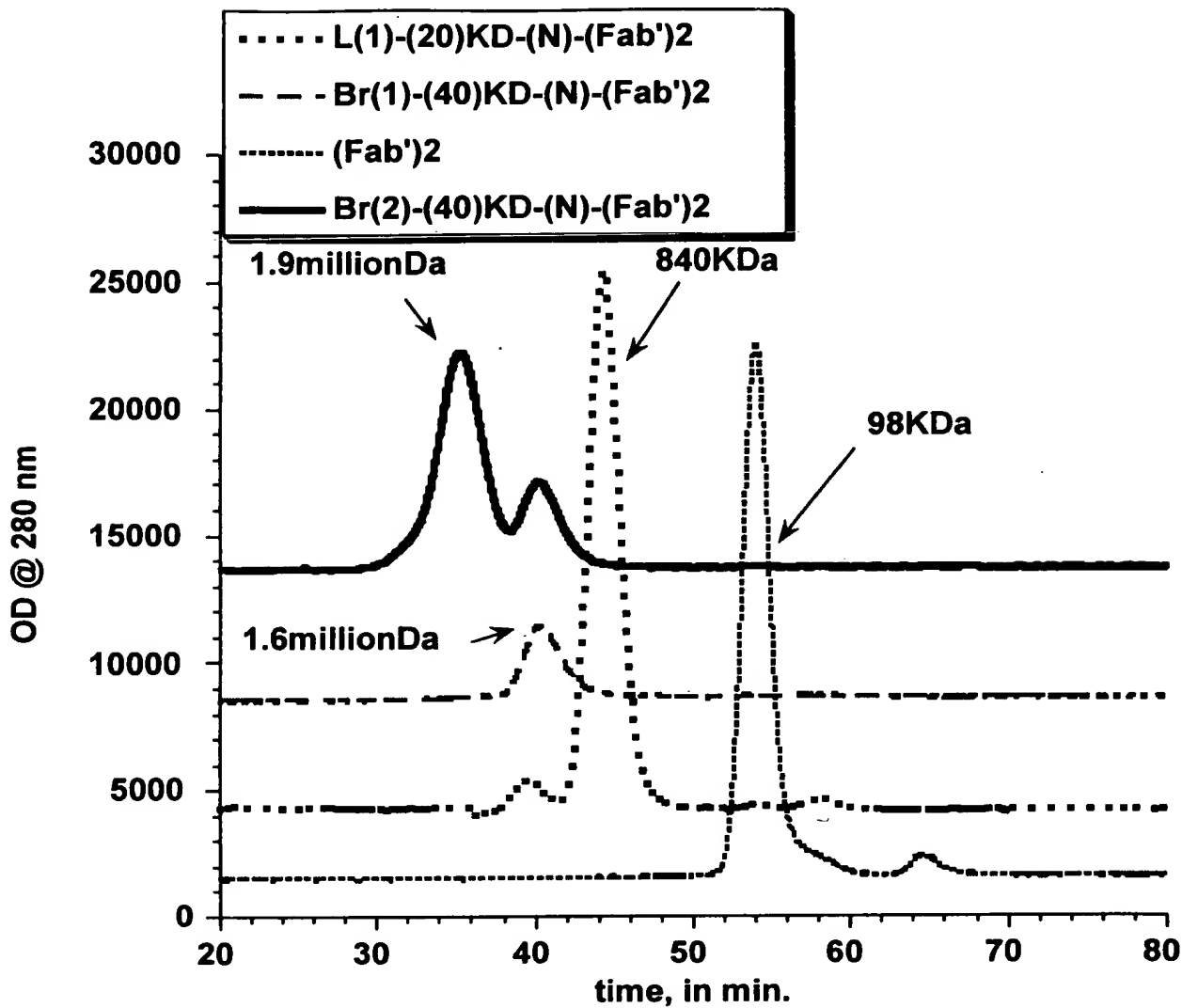


FIG. 62



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

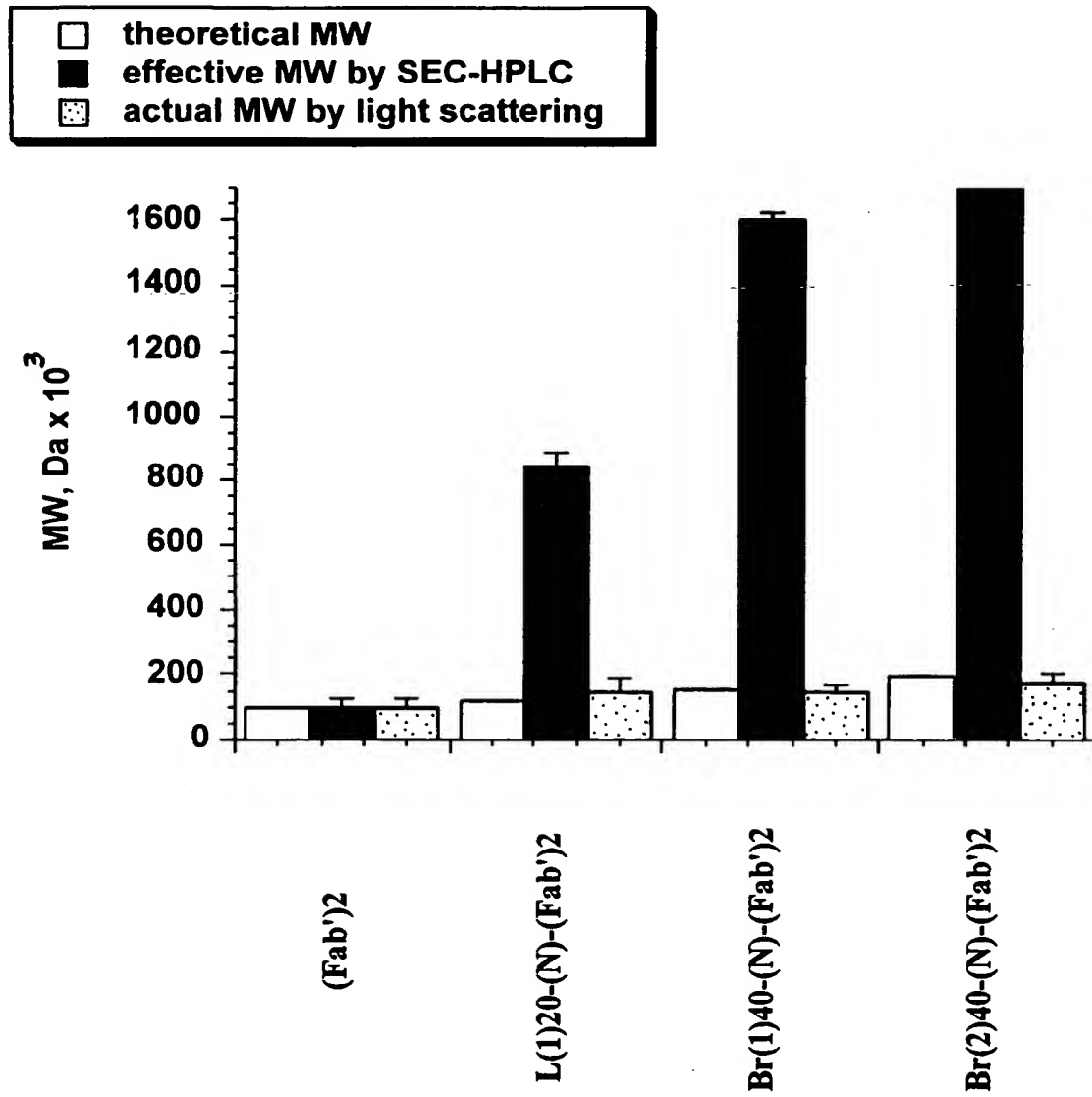


FIG. 63



10/21/02

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

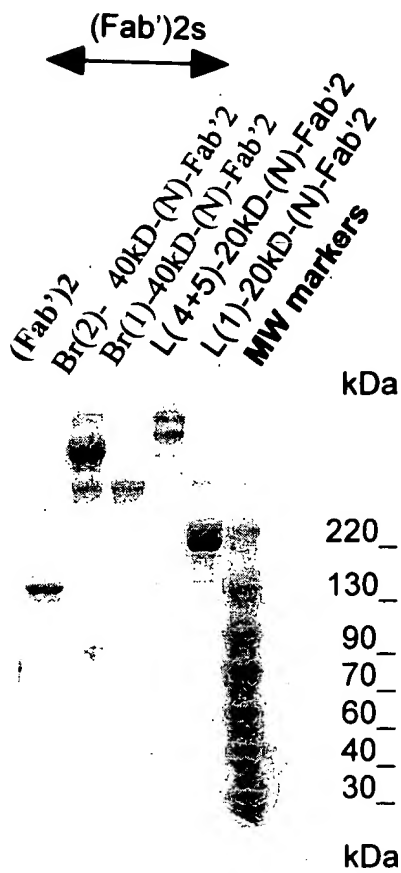


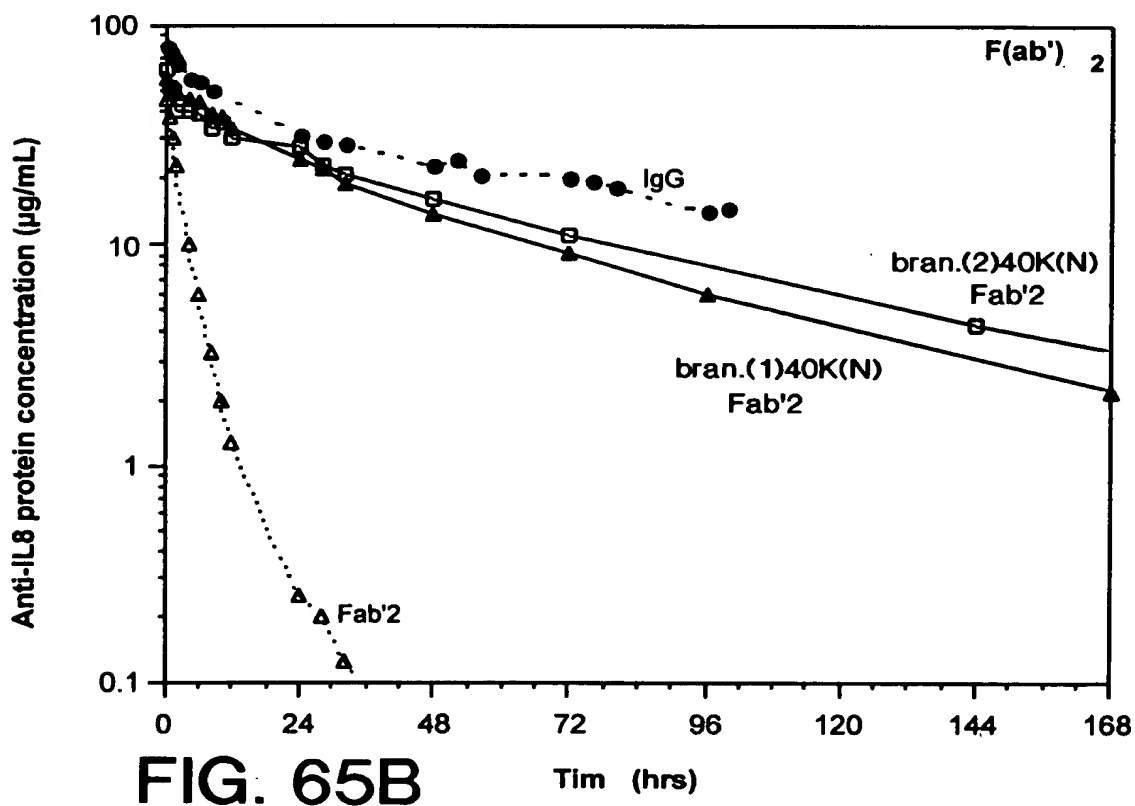
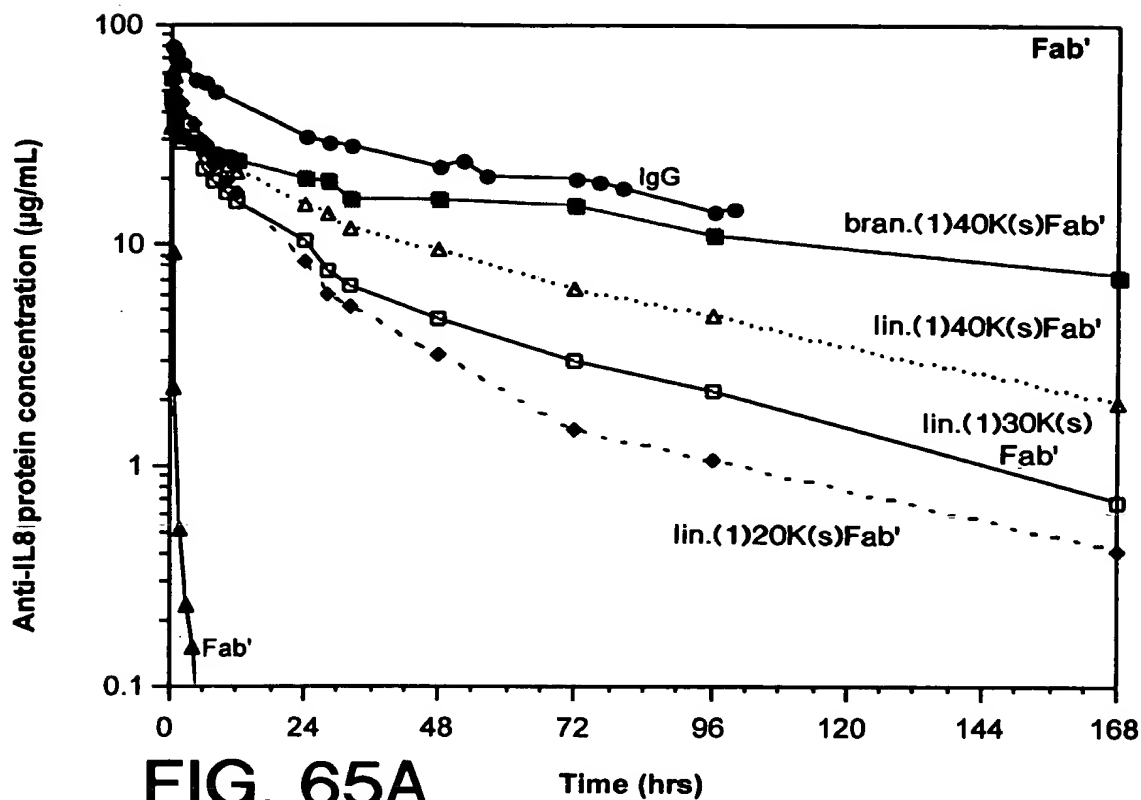
FIG. 64



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

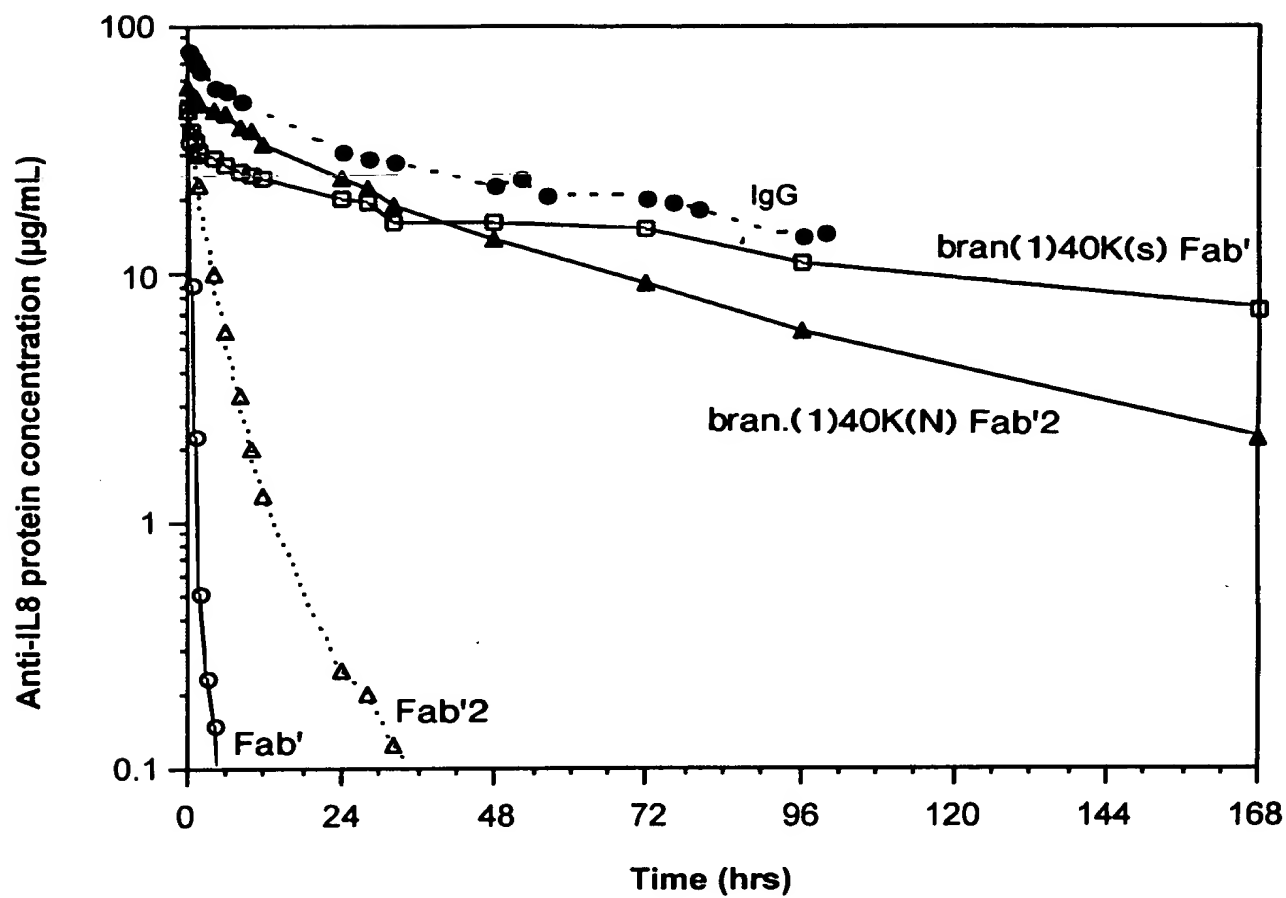


FIG. 66



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

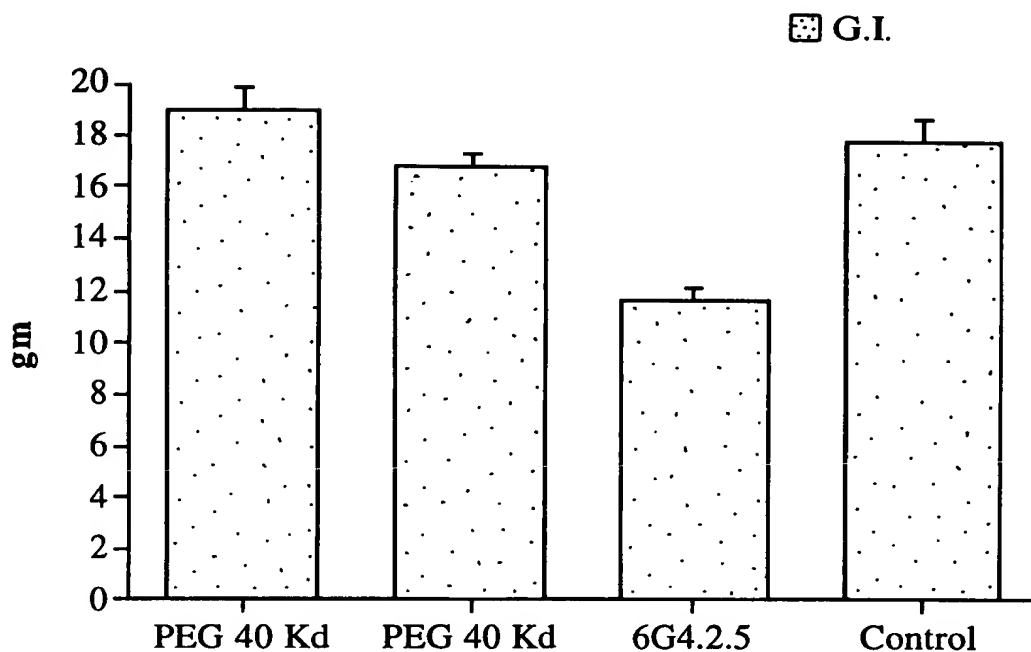


FIG. 67

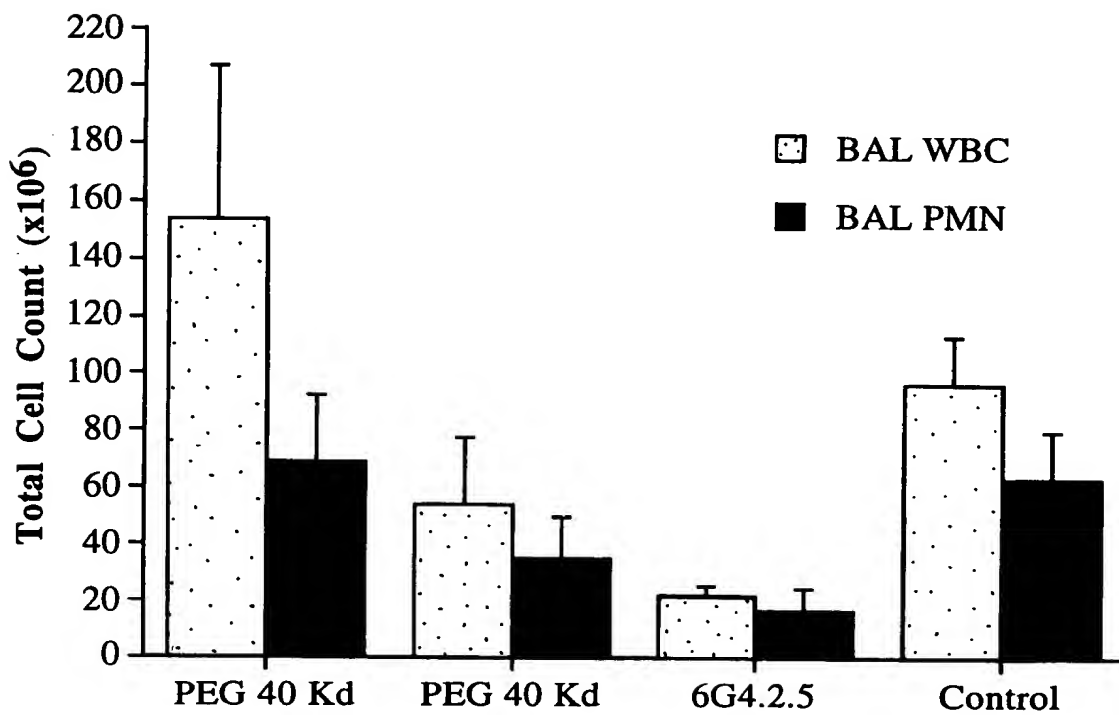


FIG. 68



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

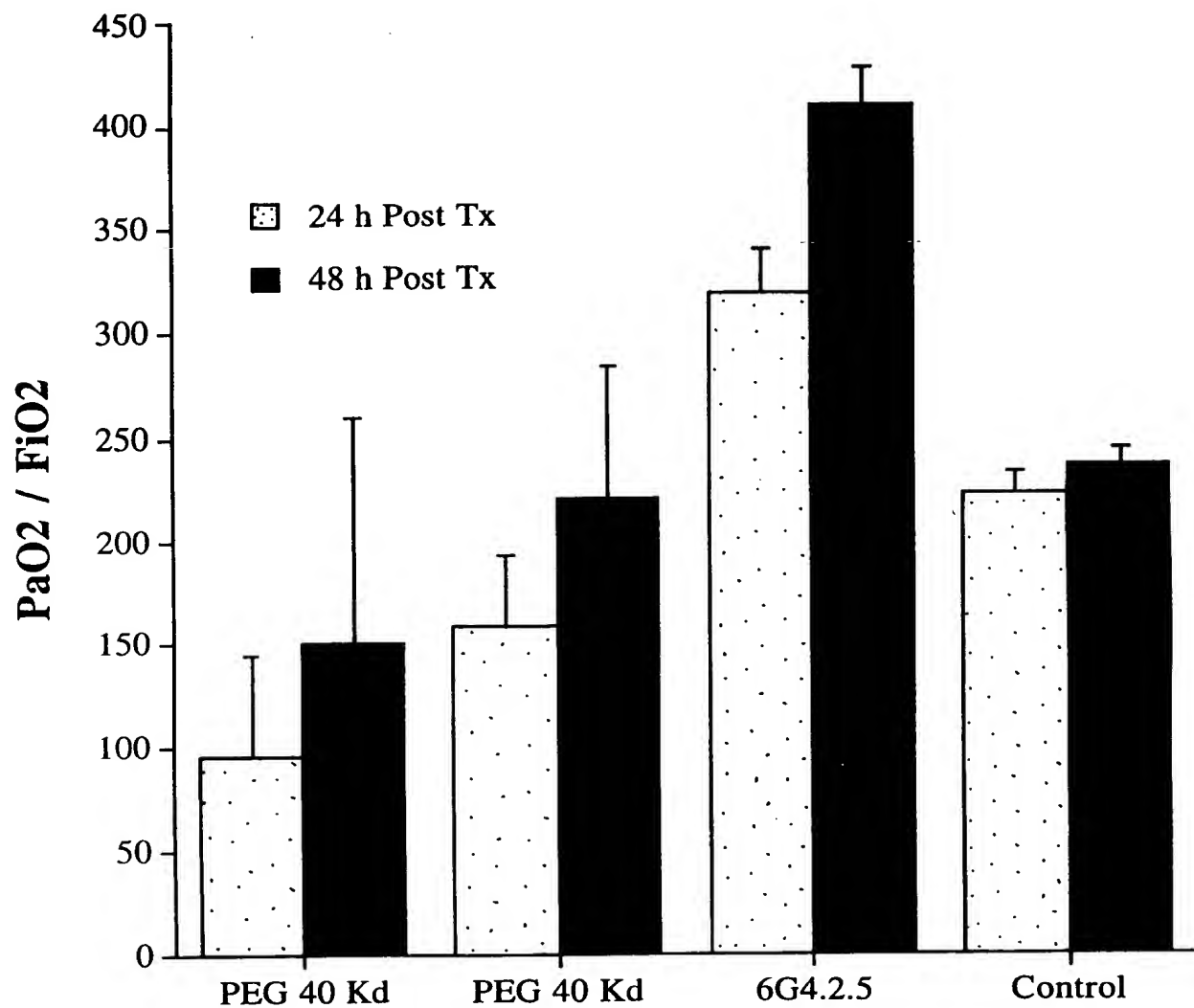


FIG. 69



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Oxygenation in 100% O₂ @24 h Post Anti-IL8 Tx

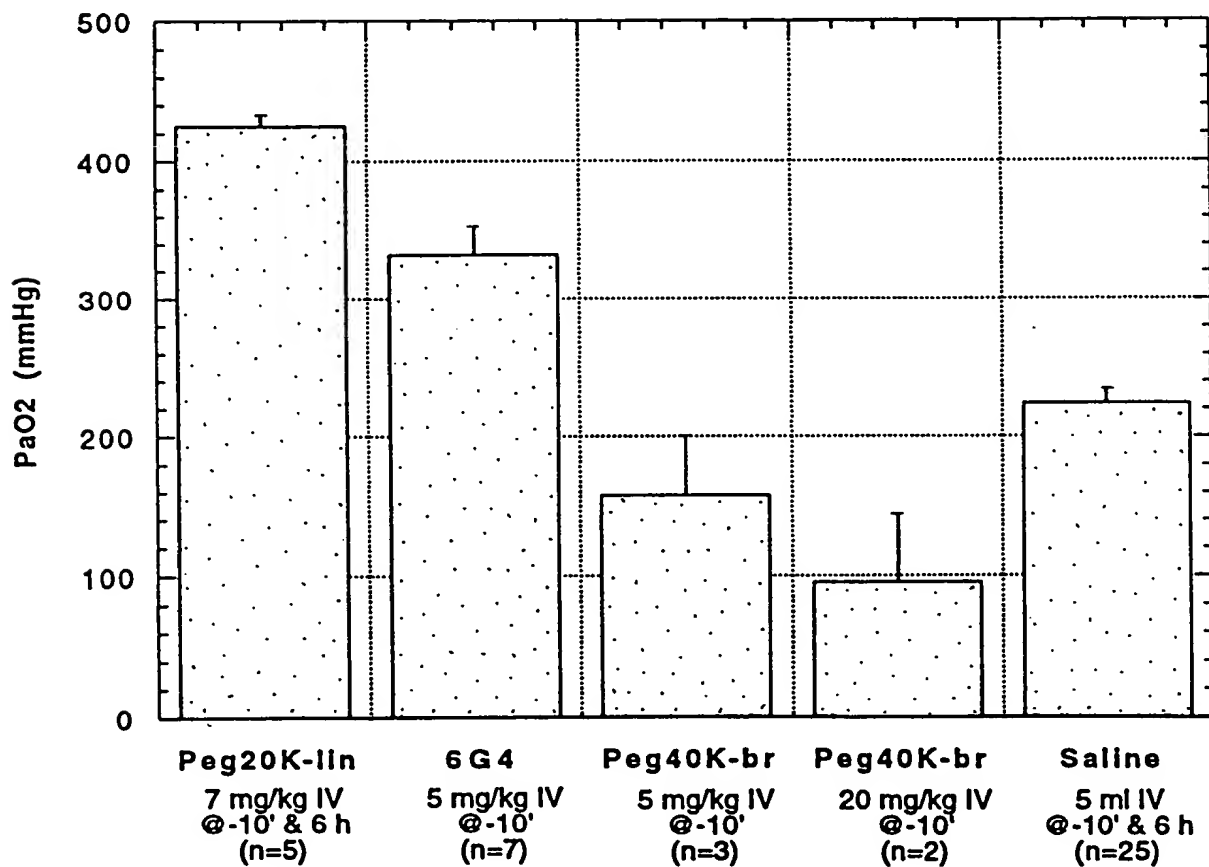


FIG. 70A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

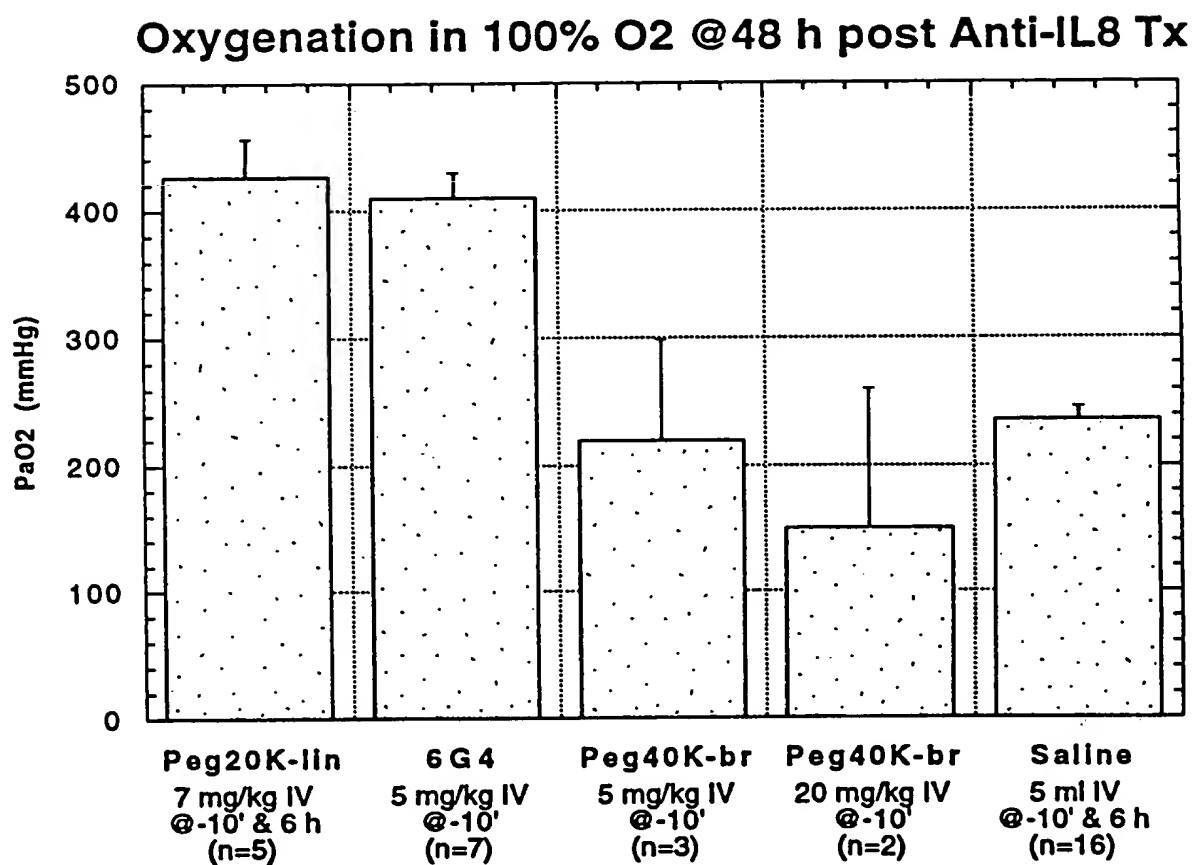


FIG. 70B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

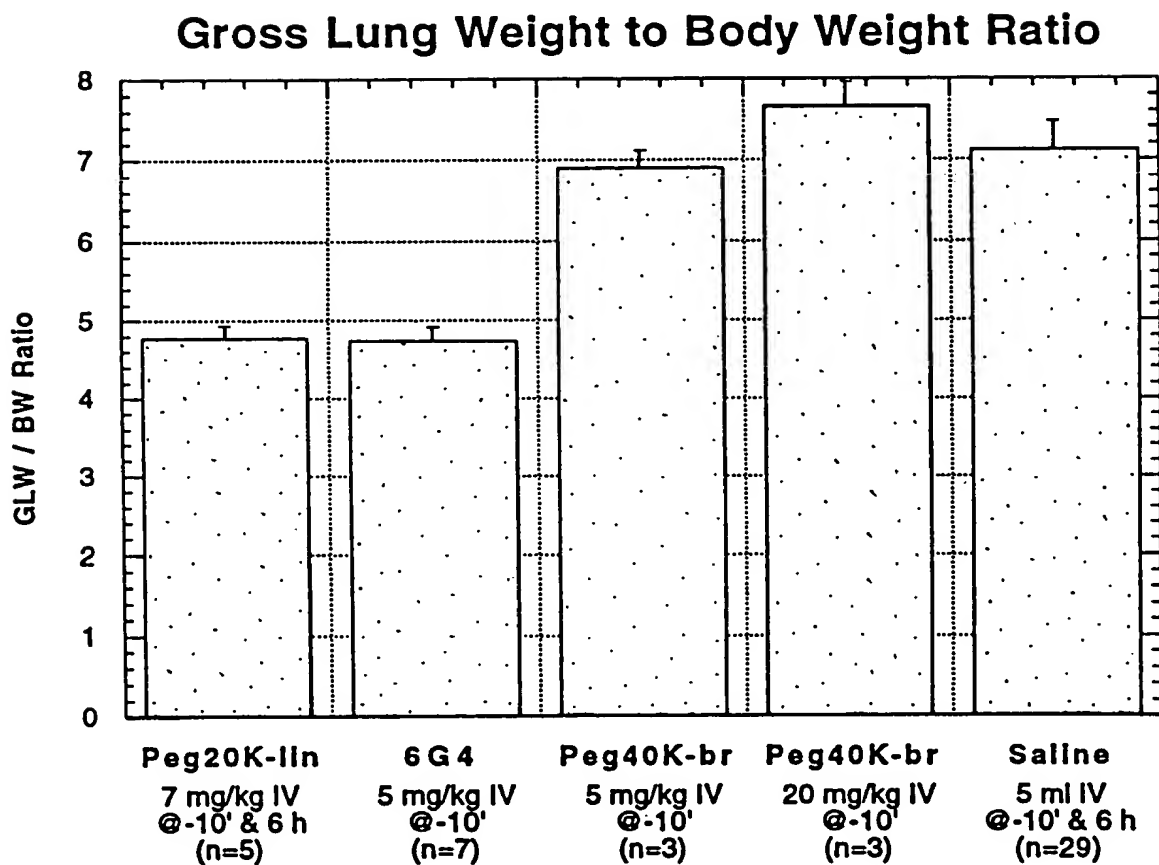


FIG. 70C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

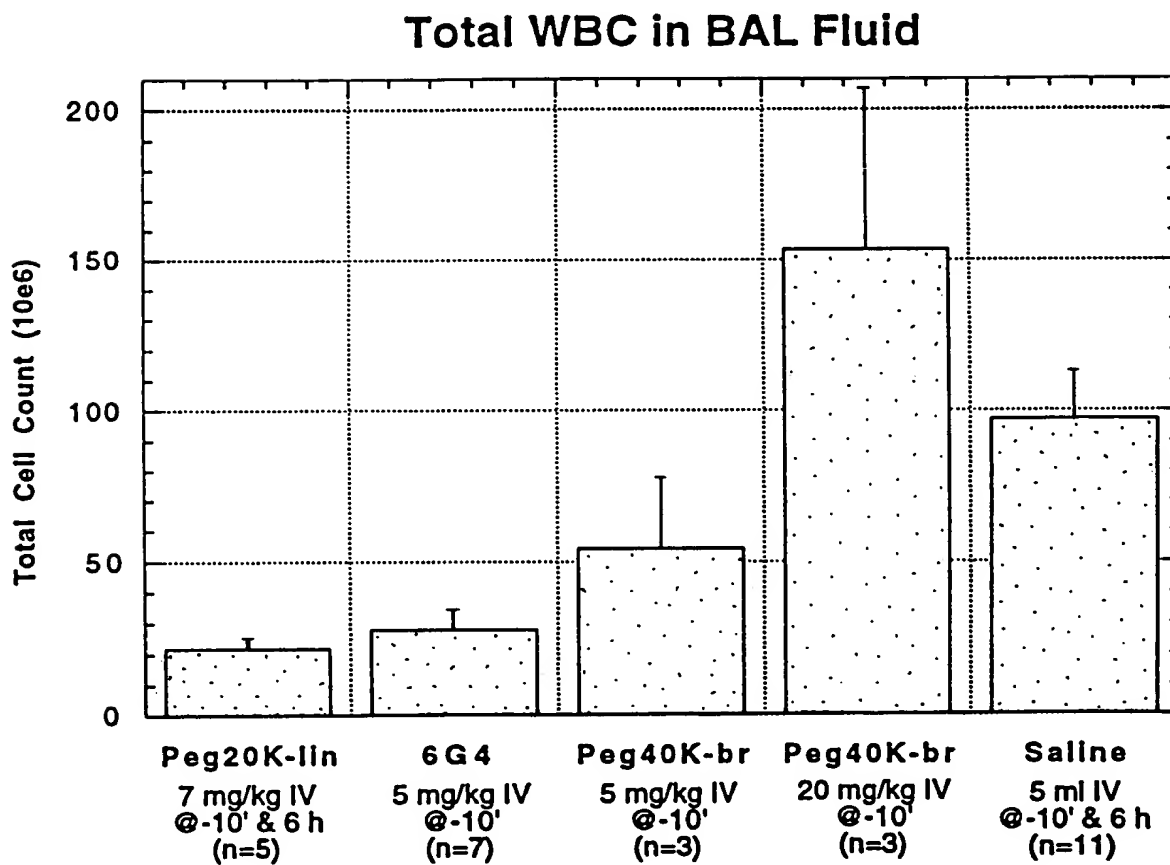


FIG. 70D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

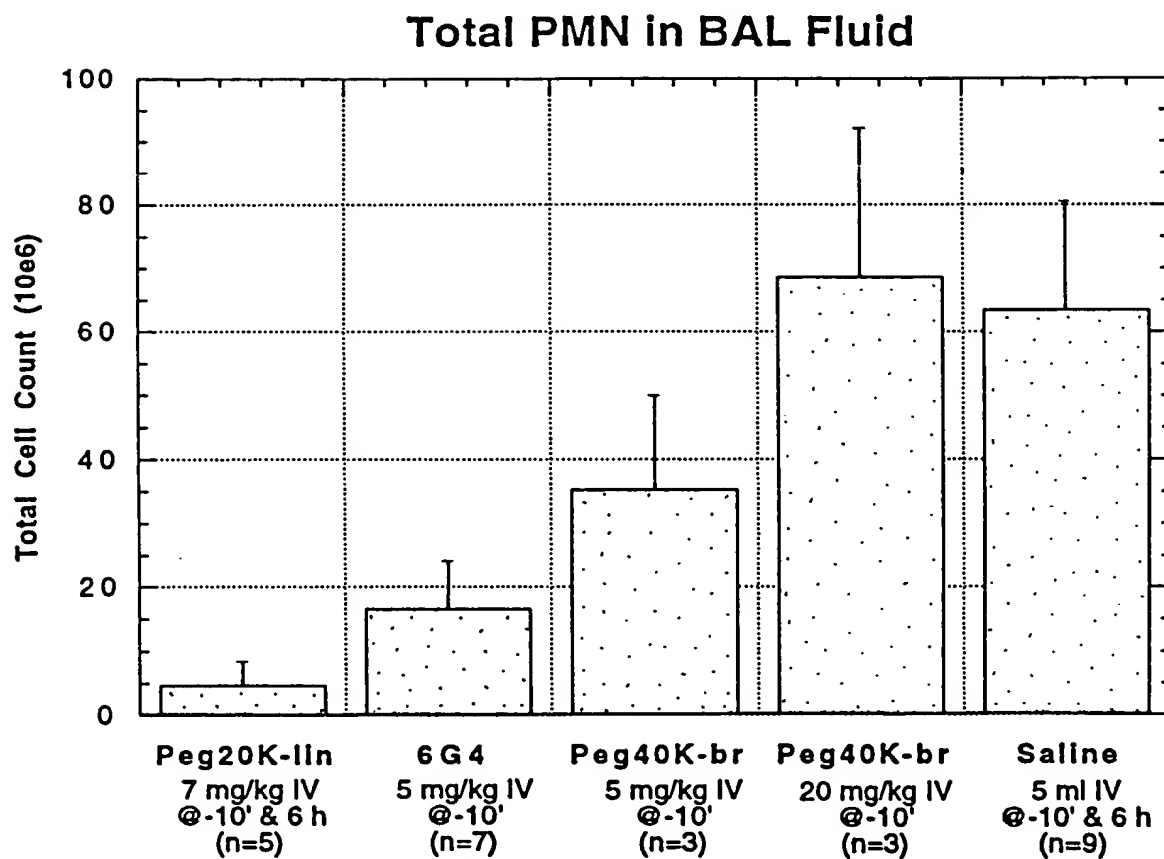
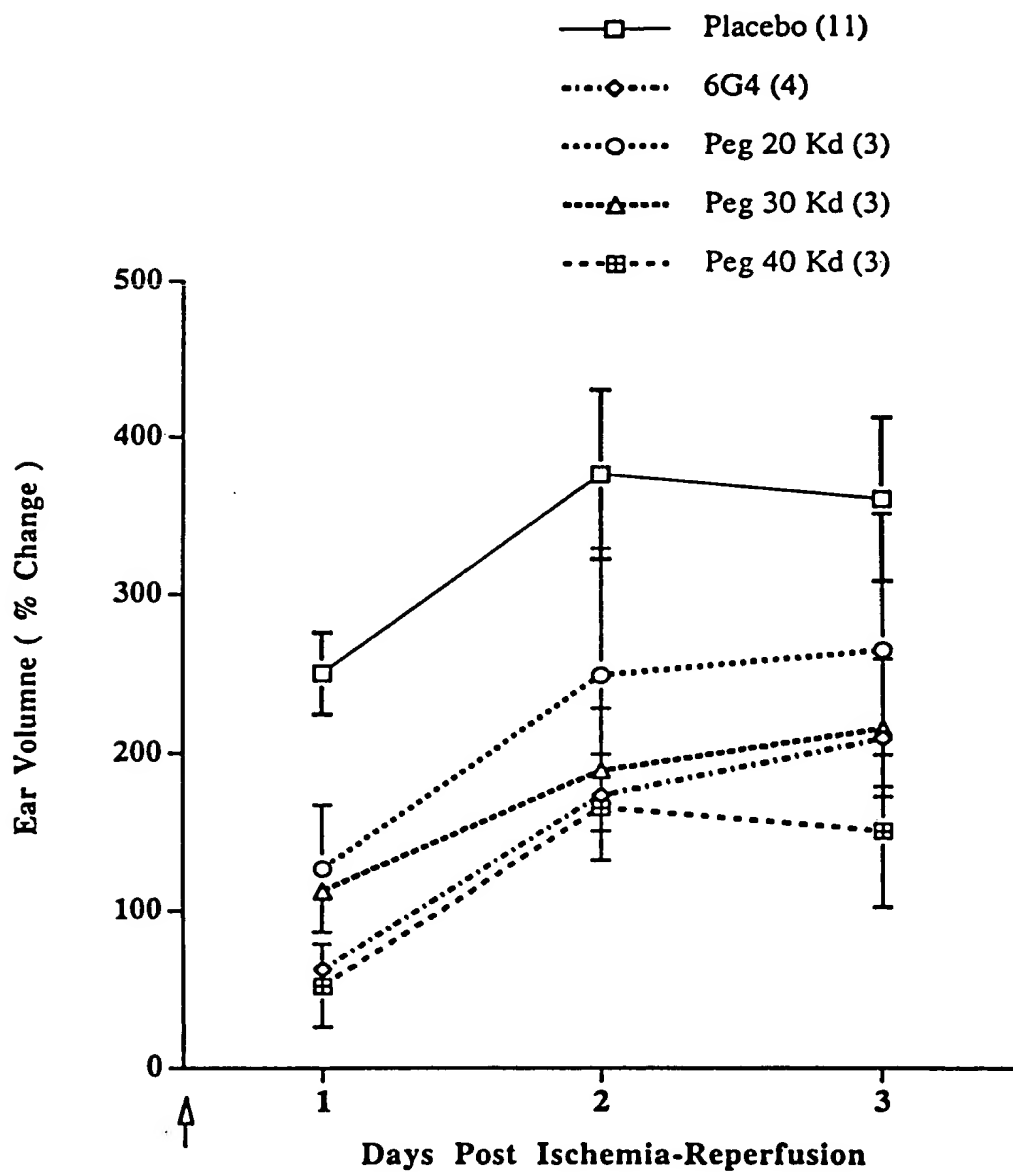


FIG. 70E



The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
Single Dose (5 mg/kg)
administered IV at time
of reperfusion

FIG. 71